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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

SEPTEMBER, 1914

ORIGINAL ARTICLES

SEVERE ANEMIA CONNECTED WITH GASTRO-INTESTINAL DISEASES.[1]

By Dr. Adolf Schmidt,

PROFESSOR OF INTERNAL MEDICINE, UNIVERSITY OF HALLE, GERMANY.

Although not aware of the frequency of pernicious anemia in the United States, I believe that in Europe it is becoming more and more frequent. When studying the different kinds and manifestations of intestinal dyspepsia, I met with more or less severe anemia, and will state the relationship existing between these two morbid conditions.

Combe, Addison, and Biermer first described certain cases of anemia, marked by their intensity and fatal issue, as idiopathic or pernicious anemia. They based their reasons for separating this particular anemia from the common type not only on the serious character of its clinical symptoms—high degree of blood changes, fever, extravasations of blood, digestive troubles, etc.—but also on the absence of any organic lesion which could be regarded as the origin of the disease and the lack of any conceivable etiology. This manner of defining a new clinical disease chiefly by negative symptoms, though corresponding to the state of science at that time, could not be satisfactory. Thus the discussion about the nature and the conception of the disease began and has continued, producing numerous facts and theories, but not at all solving the problem.

[1] Delivered before the Harvey Society, October 18, 1913.

One of these facts is the discovery, made by Russian and Danish authors, especially by Rosenquist, Schaumann, and Talquist, that infection with bothriocephalus is able to cause a form of progressive anemia which by no means can be separated from Biemer's pernicious type. With that the idiopathic or primary character of the disease became doubtful. But though there were found subsequently other causes of the disease, as syphilis (Fr. Müller), pregnancy (Gusserow), etc., the remaining number of unexplained cases was still large.

In interpreting these cases from 1900 to the present time, two different theories are mostly discussed: according to one of them, inaugurated by Paul Ehrlich, the characteristic sign of the disease is the megaloblastic degeneration of the blood-forming structures; the other, advocated by W. Hunter, starts from the hemolytic nature of the disease and supposes its origin to be found in a more or less specific affection of the gastro-intestinal tube.

Ehrlich's hematological studies, by means of differential staining, led him to the conclusion that a distinct type of bone-marrow change, which causes the appearance of large and intensely colored, partially nucleated red corpuscles—megalocytes and megaloblasts—cell forms which under normal conditions appear only in embryonic life, is not only the essential symptom but even the cause of pernicious anemia. He and his followers (Lazarus, Engel, Naegeli, and other hematologists) speak of pernicious anemia only if this sign and some other blood changes, as increased color-index, poikilocytosis, diminished number of leukocytes, with comparative increase of lymphocytes, are evident.

There can be no doubt that by accepting Ehrlich's theory the conception of the disease, given by Addison and Biemer, is changed to some extent, for clinical observation shows that megaloblastic degeneration may be present in some cases of common (secondary) anemia and absent in others belonging to the idiopathic group. The megaloblastic type of blood formation, though a characteristic symptom of the disease, as is the pigmentation of internal organs and the tendency to hemorrhages does in no way explain the etiology. If pigmentation is the cause of hemolysis, the changes in blood formation must be taken as reactions of the bone marrow to the unknown cause of hemolysis (Naegeli).

Hunter was the first to perceive the hemolytic nature of pernicious anemia. After him this form is distinguished from all other forms by the excessive presence of iron in the liver, due to the more or less continuous destruction of red corpuscles within the portal circulation. Though he could not prove the presence of the hemolytic process itself nor produce the hemolytic substance from the organs, he tried to confirm his theory by indirect arguments, especially by demonstrating the constant presence of glossitic lesions, which he supposed to be caused by streptococcic

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infection, and by finding an increased amount of aromatic sulphates and other products of intestinal putrefaction in the urine of his patients.

Hunter's observations, at first neglected in consequence of the attention generally bestowed upon Ehrlich's studies, have found valuable support through E. Grawitz and other clinicians. But his theory could not be accepted before the supposed hemolytic principle was brought into evidence. This was done in 1907 by Tallquist in bothriocephalus anemia, the best studied form of enterogenous anemia. Only a small percentage of patients harboring tape-worm suffer from anemia. Tallquist estimates the occurrence to be less than 1 per cent. Though this disease in its severer forms shows all symptoms of pernicious anemia, the blood is by no means always megalocytic or even megaloblastic. Sometimes in the beginning there are found glossitic lesions analogous to those described by Hunter. Nitrogen metabolism is periodically altered so that increased decomposition of albuminates must be accepted (Rosenquist). The substance which causes hemolysis is produced in the tape-worm itself, not in the healthy one, but in degenerated parts of it by an autolytic process. It is a cholesterin ester of oleic acid, which in small quantity also may be obtained from different normal organs. If the bothriocephalus is removed by efficient treatment the patients may entirely recover, but in some cases there still remains an increased tendency to the recurrence of anemia (Schaumann).

Bothriocephalus is not the only worm the presence of which gives rise to anemia, as the hook-worm, which sucks blood from the mucous membrane, thus leads to successive anemia. But as it produces no toxin, the megaloblastic blood degeneration is missing. On the other hand, there have been described some undoubted observations of the pernicious form connected with the common tape-worm (Tenia saginata) and with trichocephalus, round-worm, and certain protozoic infections. Even in tropical sprue an anemic condition of severe character is sometimes seen, although exact investigations of blood changes are not yet published.

Regarding the hemolytic nature of bothriocephalus anemia, it is natural to suppose similar conditions in other forms of anemia connected with gastro-intestinal disorders. Besides the large class of unexplained idiopathic anemias, there are two more morbid states which from this point of view excite our interest—namely, the coincidence of a small non-ulcerated stomach cancer, with progressive anemia of the megaloblastic type, and the development of the same pernicious form in the course of cicatricial stenosis of the small intestine.

As regards the first condition, the fact is well known that the so-called cancer anemia appears especially in cancers of the gastro-intestinal tract. Though the blood generally does not show the

One of these facts is the discovery, made by Russian and Danish authors, especially by Rosenquist, Schaumann, and Talquist, that infection with bothriocephalus is able to cause a form of progressive anemia which by no means can be separated from Biemer's pernicious type. With that the idiopathic or primary character of the disease became doubtful. But though there were found subsequently other causes of the disease, as syphilis (Fr. Müller), pregnancy (Gusserow), etc., the remaining number of unexplained cases was still large.

In interpreting these cases from 1900 to the present time, two different theories are mostly discussed: according to one of them, inaugurated by Paul Ehrlich, the characteristic sign of the disease is the megaloblastic degeneration of the blood-forming structures; the other, advocated by W. Hunter, starts from the hemolytic nature of the disease and supposes its origin to be found in a more or less specific affection of the gastro-intestinal tube.

Ehrlich's hematological studies, by means of differential staining, led him to the conclusion that a distinct type of bone-marrow change, which causes the appearance of large and intensely colored, partially nucleated red corpuscles—megalocytes and megaloblasts—cell forms which under normal conditions appear only in embryonic life, is not only the essential symptom but even the cause of pernicious anemia. He and his followers (Lazarus, Engel, Naegeli, and other hematologists) speak of pernicious anemia only if this sign and some other blood changes, as increased color-index, poikilocytosis, diminished number of leukocytes, with comparative increase of lymphocytes, are evident.

There can be no doubt that by accepting Ehrlich's theory the conception of the disease, given by Addison and Biemer, is changed to some extent, for clinical observation shows that megaloblastic degeneration may be present in some cases of common (secondary) anemia and absent in others belonging to the idiopathic group. The megaloblastic type of blood formation, though a characteristic symptom of the disease, as is the pigmentation of internal organs and the tendency to hemorrhages does in no way explain the etiology. If pigmentation is the cause of hemolysis, the changes in blood formation must be taken as reactions of the bone marrow to the unknown cause of hemolysis (Naegeli).

Hunter was the first to perceive the hemolytic nature of pernicious anemia. After him this form is distinguished from all other forms by the excessive presence of iron in the liver, due to the more or less continuous destruction of red corpuscles within the portal circulation. Though he could not prove the presence of the hemolytic process itself nor produce the hemolytic substance from the organs, he tried to confirm his theory by indirect arguments, especially by demonstrating the constant presence of glossitic lesions, which he supposed to be caused by streptococcic

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infection, and by finding an increased amount of aromatic sulphates and other products of intestinal putrefaction in the urine of his patients.

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characteristic signs of toxic bone-marrow reaction, hemolytic substances comparable to those of the bothriocephalus body have been separated from cancerous tissue by Kullmann, Tallquist, and others. They may be, but seldom are strong enough to overcome the regenerative power of the blood-forming organs. In the cases referred to, the postmortem examination did not exhibit any other cause of the anemia, as, for instance, inflammation of the mucous membrane, cancerous degeneration of the bone marrow, etc. v. Noorden, Israel, Scott, Bloch, Lazarus, Nauer have observed such cases, and I can add two of my own. Shall we regard this coincidence as chance? Are there two different diseases coexistent? I think it is difficult to deny entirely any connection between them.

The second condition, cicatrised tuberculous stenosis of the small intestine, accompanied with pernicious anemia, was first described by Faber and Borchgrevink. Most of the cases hitherto known showed no fresh ulcerations nor any notable inflammation. In my own two observations even microscopic investigation demonstrated only the same state of insignificant lymphocytic infiltration of the mucous membrane, as in other cases of pernicious anemia. Neither the preëxisting tuberculous ulceration nor the scars, but only the irrigation of the intestinal walls following the chronic retention of the contents, can be regarded as the etiology.

The group of unexplained cases of pernicious anemia in relation to gastro-intestinal troubles now claims our attention. Biemer has described certain digestive disturbances, as anorexia, gastric discomfort, weak digestion, and periodic diarrhea, as the chief symptoms of the disease called after him; but he regarded them as consequences of the anemia, as did succeeding observers except Hunter. Hunter says: "A history of antecedent gastric or intestinal disturbances was found in each of twenty-five cases. In no case were these of sufficient character or intensity to account for the supervention of such an intense degree of anemia. The various disturbances connected with this tract have an important sigficance, not as a cause of the disease, but as symptoms of the gastric and intestinal infective lesions associated with the disease." In other words, anatomical lesions, especially the infective glossitic changes, are the chief factors; the digestive troubles are only the mild manifestations of these lesions.

According to the more physiological point of view of modern clinical investigation we will first consider these functional disorders. The fact of the constant absence of hydrochloric acid in the gastric contents of all patients suffering from pernicious anemia was somewhat neglected until Martius found out that we had to deal not only with a defect of hydrochloric acid, but of the whole gastric digestion, *i. e.*, with achylia gastrica. Even this fact did not attract much attention, for by the more common use of the stomach-tube it soon became evident that many persons who

have no gastric juice do not suffer from any digestive trouble, and that this condition does not depend necessarily on atrophy of the gastric glands. But the conception has considerably changed. Since Oppler and Einhorn first described chronic diarrheas following gastric achylia the different forms of gastrogenous intestinal dyspepsia have become an object of clinical interest, the consequences of which cannot yet be fully estimated. Faber, who analyzed 207 cases of achylia, found in 22, or 11 per cent., marked signs of pernicious anemia, and in 22 others a hemoglobin o less than 50 per cent. While the anemia in these latter cases only showed the character of a serious chlorosis, in the others all the blood changes of the pernicious form were present; increased color-index, poikilocytosis, leukopenia, and megaloblastic degeneration of the red corpuscles. Furthermore, Faber observed a number of patients suffering from severe anemia, whose achylia had already existed and had been proved many years before they fell sick with anemia. This fact led him to the conclusion that pernicious anemia is not, as generally supposed, the cause of gastric achylia, but, on the contrary, the result of it.

Coming now to the intestines, it was Grawitz who, following Hunter's suggestion, attached most weight to enterotoxic products, which he supposed to result from insufficient or faulty denaturation of the albuminates. Unfortunately, he also was unable to produce any argument which could confirm his theory. I therefore first undertook to study the frequency and kind of the intestinal troubles, mentioned by most authors as a symptom of the disease, but not yet analyzed by anyone.

Among my patients suffering from idiopathic pernicious anemia there were sixteen, the third part of all observed, who showed more or less marked signs of intestinal disorders. They mostly had periodic diarrhea, or diarrhea alternating with constipation. Generally the diarrhea was of an insignificant degree, and was not accompanied with colicky pains.

When examined by means of my test-diet or similar food, the feces were of a pulpy consistency, and had an offensive odor, which sometimes was distinctly sour. Corresponding to that the reaction was either markedly alkaline or acid, the normal test-diet stool being nearly neutral. When ground up with water to a fluid consistence, often small flakes of mucus could be seen, whereas larger particles were constantly missing. A few times the whole mass showed a mucous condition, though no flakes could be isolated. Chemical tests showed that this condition was caused by the presence of a large quantity of nucleoproteid, a product of the intestinal epithelium, which under normal conditions appears only in small quantity.

As to the remains of food, connective tissue was often found, due to the lack of gastric juice. Macroscopic remains of muscular

tissue seldom could be seen, but often increased quantities of microscopic muscle fragments. Starch granules colored blue with iodine and numerous needles of fatty acid and soaps were easily defined by the microscope. The fermentation test at times was positive.

Interpreting these facts we have to deal with a kind of intestinal dyspepsia, sometimes associated with an irritation of the surface epithelium and periodically bringing about a transitory inflammation of the mucous membrane. These are the same conditions as found in other non-anemic cases of gastric achylia; they offer the real features of what are called gastrogenous dyspepsia. As in all these forms their appearance changes, now present for a shorter or a longer time, now ceasing suddenly and permitting stools of completely normal character or a state of mild constipation. Therefore it may happen they are only identified by carefully inquiring into the previous history, as they are absent during the period of observation. In the majority of my cases transitory diarrhea and gastric achylia, which was present in all my cases except one, preceded the development of the anemia many years.

There is marked harmony between my observations and those of Faber, especially as to the pre-anemic digestive troubles. Endeavoring to answer the question in which way achylia may lead to anemia, Faber believed it to be by way of the intestine. According to his suggestion the lack of hydrochloric acid gives rise to the establishment of hemolytic bacteria in the small intestine, but he did not prove either the existence or the nature of the supposed intestinal disorders. This was omitted by all the earlier authors, as, for instance, Martius, who sought the cause of pernicious anemia in atrophy of the mucous membrane, proceeding from the stomach to the duodenum and small intestine. As to my experience, not only is the frequency of intestinal dyspepsia in pernicious anemia striking, but even more so in the frequent occurrence of various degrees of anemia in all forms of chronic intestinal dyspepsia. The percentage of serious forms of anemia occurring in the course of gastrogenous dyspepsia is much higher than that occurring in simple achylia not connected with diarrhea. Thus the common non-specific intestinal dyspepsia forms the missing link between achylia and pernicious anemia.

We cannot here thoroughly discuss the theories concerning the real causes of intestinal disorders following gastric achylia. Faber's suggestion, based on the passage of pathogenic bacteria through a stomach not containing hydrochloric acid, a theory established long ago by Baumann and his pupils, is indeed useful, because the condition of chronic intestinal dyspepsia cannot be understood without the coöperation of bacterial fermentation. But surely the lack of hydrochloric acid cannot by itself entirely explain the problem. The connective tissue and other food remains which

are not dissolved in the achylic stomach contents may be accused with more probability, as they are not only a lurking place, but also a good culture medium for decomposing bacteria, which under these conditions settle in the duodenum. Together with burdening of the intestine with insufficiently dissolved food, they slowly lead to a state of exhausted pancreatic digestion, which can sometimes be proved by the appearance of unchanged nuclei in the feces.

Turning now to the anatomical lesions, the glossitic changes known as Hunter's tongue can be observed in the majority of cases. Microscopic investigation shows proliferation of the epithelial covering alternating with atrophic spots, fissures, mild degrees of lymphocytic exudation, and other signs of chronic inflammation. Streptococcic invasion, found by Hunter, can only be regarded as accidental. It may also be noticed that irritability of the tongue, corresponding to the characteristic appearance, sometimes precedes the anemia (Matthes).

Faber and Bloch, who studied the microscopic structure of the stomach in achylia, found the lymphatic follicles enlarged and indistinctly shaped, lymphocytes more or less spread through the mucous membrane, and the glands diminished in number and size, doubtless signs of chronic inflammation, but no atrophy.

As to the intestine, the question introduced by Nothnagel as to whether an atrophic state of larger parts of the mucous membrane, like those occasionally seen in the stomach, are in any way to be found, can be answered in the negative. Though the macroscopic features of a thin, pale, and transparent intestinal wall, especially met with in cases of pernicious anemia, seems to disprove that careful microscopic examination of the whole intestine, prepared immediately after death, shows only the same pathological changes as in the stomach. Even by comparing the weight of the whole mucous membrane with that of a normal one, and by counting the number of Lieberkühn's glands in sections from different parts, Meyer and v. Lippmann in my laboratory, agreeing with Faber and Bloch, found no atrophy. There were the same signs of a slight chronic inflammation of the mucous membrane as found in the stomach. Only once did I observe a fresh inflammation in the lower part of the ileum.

Gathering up these facts, we must conclude that the anatomical lesions corresponding to the functional disorders do not show any specific character, that they must be regarded rather as the result than as the cause of the digestive disturbances. Hunter's suggestion of a primary infectious origin of pernicious anemia is proved neither by anatomical nor by bacteriological facts.

But the fact of coincidence of the gastro-intestinal lesions with the anemic condition cannot prove their causal connection. Are there any arguments to make evident the hemolytic nature of

these lesions? Though it is well known, and can easily be demonstrated, that the blood taken from the peripheral veins in pernicious anemia does not show or seldom shows signs of hemolysis, such as colored serum or decreased resistance of the red corpuscles to salt-solution, there are some remarkable facts supporting the theory of a hemolytic agent especially circulating in the portal venous system. The first, produced by Hunter himself, is the excessive accumulation of iron in the liver, which is more than three times as great as under normal conditions, and does not bear a correct relation to the amount of iron in the spleen and the kidneys. The other fact, exhibited by M. B. Schmidt and communicated by Matthes, is the reddish (hemolytic) color presented only by the portal lymph vessels and lymph nodes in patients who died from pernicious anemia.

Accepting the suggestion of a hemolytic agent entering into the portal system, the question arises whether it is produced in the chyme or in the mucous membrane of the bowels. The presence of an increased amount of hemolytic substances in the intestinal contents or in the feces, if ever proved—as it has not been—cannot satisfy us, because the decomposition of almost all sorts of food sets free transitory traces of oleic acid. This acid is shown by Tallquist and Faust to be an efficient hemolytic substance; the normal epithelium must be able either to withstand such a noxious substance or, if absorbed, to destroy its toxic character by changing its structure. By the same reason the researches of Lüdke and Fejes, who extracted hemolytic substances out of the different intestinal bacteria, especially from the Bacillus coli, isolated from pernicious anemia, do not explain anything, as so far there is no evidence that the bacteria penetrate the covering epithelium and grow within the mucous membrane.

On the other hand, Korschun and Morgenroth produced hemolytic lipoids from different normal organs; for instance, from the mucous membrane of the intestine, the pancreas, etc. Starting from that fact, Berger and Tsuchiya in two of our cases of pernicious anemia immediately after death prepared the mucous membrane of the whole gastro-intestinal tube. The lipoids extracted from the stomach, and even more from the small intestine, showed a hemolytic power about ten times higher than those of normal organs. I believe this result to be of great importance, although Ewald and Friedländer could not confirm it. But they omitted to examine fresh organs.

Remembering the microscopic signs of chronic inflammation, mentioned before, we are justified in supposing certain degenerative changes in the mucous membrane of the small intestine which may set free hemolytic substances. It is obvious that the constant absorption of even a small quantity by an organ, especially des-

tined for absorption, can exhaust the reproductive power of the bone marrow.

Another fact, just stated by Kabanow in my laboratory, may confirm this suggestion. Working with the new Abderhalden method of proving the origin of diseases by searching for the so-called specific protective ferments circulating in the blood, Kabanow in three cases of pernicious anemia found the mucous membrane of the small intestine regularly, that of the stomach only once, but that of the colon, liver, etc., never decomposed by the serum. This means that the small intestine and in a lesser degree also the stomach, undergoes degeneration.

If the experiences hitherto spoken of seem to confirm the causal connection between certain digestive disturbances and the development of pernicious anemia, I do not believe that all cases of this disease have this origin. Only one-third of the patients suffering from pernicious anemia show marked intestinal troubles, and the number of dyspeptic persons who acquire severe anemia is not higher. Moreover, experience shows that the anemic condition when once developed, does not always go parallel with the intestinal troubles. While the latter improve and relapse, the anemia often maintains its progressive character even when the digestion has improved under careful treatment. Schaumann studied the fate of his patients who recovered from bothriocephalus anemia and found that part of them still inclined to relapsing anemia. This observation and other circumstances induced him to believe that a constitutional state forms the basis upon which different lesions may give rise to pernicious anemia. Indeed, Bartlett, Pateck, Matthes, and others, saw striking examples of family or hereditary development of the disease. Pernicious anemia can be produced also by causes which have no connection with the gastro-intestinal tube, such as lues, pregnancy, septic infection, chronic nephritis, etc., though the intestine as the chief place of absorption prevails. If the experiment newly made by Eppinger and Delcastello, that extirpation of the spleen is able to cure certain cases of pernicious anemia, should be confirmed in the future, we must deal with the possibility of an accumulation of the hemolytic agent in the spleen, as Banti supposes to take place in the disease called after him.

The blood changes of pernicious anemia, interpreted by the hematologists as a degeneration of blood formation, leads to the same suggestion of a various etiology of the disease. There is no proof that only toxic irritation of the bone marrow produces the megaloblastic type of blood formation. Every sort of exhaustion can do the same. Often the first attack can be combated by stimulating the blood-forming organs with arsenic. If the cause of permanent blood dissolution is at once removed the anemia may disappear.

It is useless to discuss a problem which cannot be solved with

our present knowledge. Turning to the more practical question, Do the facts in any way influence our treatment of pernicious anemia? Grawitz, who first accepted Hunter's theory, based his opinion more on his successes in treating the anemic with a carefully composed diet and with systematic washing of the stomach and colon than on pathological investigations. We all know the difficulties of feeding these patients. The irritability of the tongue and stomach is extreme, and makes them refuse all except soft food. Regarding the constant lack of hydrochloric acid in the stomach and the intestinal dyspepsia depending on it, we can give some rules which must be observed in the diet. The first is to banish all irritating substances, such as salt, spices, too hot or too cold food, sparkling drinks, high percentage alcoholics, etc. All food must be minutely chopped or mashed because the stomach, which by its juice should assimilate the injested material, does not functionate as it should. By the same reason all raw food, as fruits, salads, raw or smoked meat, etc., are not permitted. Whatever is eaten must be thoroughly cooked or grilled.

As to the combination of the food, I do not agree with Grawitz, who, fearing that the decomposition of albuminous material could supply the hemolytic agent, put his patients on a vegetarian regime. Personally, I do not prefer any particular food, but adapt the diet in each case to the report of the feces examination, which must be repeated at least every other day. If the stool shows fermentation of carbohydrates (acid reaction, remains of starch and iodophilous bacteria, production of gas in the thermostat), all vegetables, potatoes, rice, bread, sometimes even sweets, must be avoided for some days. Later, under control of the feces they may be allowed. On the other hand, evident putrefaction of the stool (with alkaline reaction, increased fragments of muscle fibers, etc.) affords restriction of the albuminous food (meat, eggs, etc.), and a more farinaceous or milk diet. Changing the regime has of itself a good effect.

As achylia of the stomach is a constant symptom of pernicious anemia, it is usual to give the patients hydrochloric acid with the meals. I sometimes exclude arsenic and other drugs, but am convinced that by regular use of hydrochloric acid not only the intestinal disorders will be diminished, but also the anemic state can be considerably improved. Grawitz, Cottan, and others have reported cases treated and cured by hydrochloric acid alone. If hydrochloric acid proves uselss, I recommend systematic washing of the stomach with physiological salt solution or salicylic acid solution (1 to 1000). More efficient are insufflations of oxygen directly into the intestine by the duodenal tube. Grawitz applied lavage of the colon with 2 per cent. salt solution, and emphasized their effect. My own experience is too slight to form an opinion about them, but I believe it is better to wash the duodenum than

the colon. I prefer these methods to the use of disinfecting drugs as none of them has proved satisfactory.

As mentioned previously, the improvement of anemia does not always keep pace with the disappearance of the intestinal disorders, yet subsequent care for the latter has a real effect also on the former. Preceding the development of anemia, the digestive troubles should be noticed as early as possible and submitted to careful treatment. Prophylaxis is always safer than healing the fully developed disease. Here, as in other branches of internal medicine, our motto must be: *Principiis obsta.*

THE RELATION OF GLYCOSURIA TO PITUITARY DISEASE AND THE REPORT OF A CASE, WITH STATISTICS.*

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The extraordinary influence of the pituitary gland upon the metabolism and development of the body is now universally conceded. Cushing[1] has grouped the disturbances of the hypophysis cerebri under the term "dyspituitarism," the manifestations being due partly to primary involvement of the gland and partly to the effects of pressure upon neighboring structures.[2] That pituitary disease, however, occasions secondary alterations in the functions of certain internal secretions is quite probable. In support of the fact that hyperthyroidism may be consequential to lesions of the hypophysis, we desire to report a case of acromegaly with glycosuria in which there were manifestations of exophthalmic goitre.

The patient, A. H., aged forty-six years, occupation cook, weight 170 pounds, and height 5 feet 9½ inches, first fell under the care of my surgical colleague, Dr. William L. Rodman, in the Medico-Chirurgical Hospital, at which time she was suffering from a gangrenous wound, inflicted by a fish bone, of the left hand. On December 12, 1913 (a few days later), the patient was referred to the medical service—to us—for study and treatment. It should be stated at the outset that the left hand continued to show swelling, was very painful, and presented a large gangrenous ulcer on the

* Read before the Association of American Physicians, at Atlantic City, May 13, 1914.

palmar surface of the index and middle fingers, with slow extension until death occurred. Polydipsia, polyuria, and glycosuria, as well as bulimia, were all prominent features throughout the illness. The percentage of sugar at first was 5 per cent., but at the end of one week it rose gradually to 7 per cent., and remained at this level until the end.

The typical symptoms of acromegaly were in evidence, as the accompanying photographs would also indicate. The hypertrophy involved both the bones, especially of the face, hands, and feet, and the soft parts, the lips being much thickened. According to the history the bones of the hands and face began to enlarge four years ago, while the glycosuria set in about two years later. An *x*-ray examination by Dr. George E. Pfahler showed marked lipping at the edges of the articular surfaces of the metacarpal bones and phalanges, such as is found in acromegaly, and also a tumor of the pituitary gland, with absorption of the clinoid processes.

The diagnosis of associated hyperthyroidism was quite apparent from the noticeable enlargement of the thyroid gland, together with tremor, tachycardia, and exophthalmos. The goitre was bilateral, although asymmetrical, soft, and elastic, but gave no suggestion of fluctuation. On auscultation a systolic arterial murmur was heard over the larger right lobe of the thyroid gland. The exophthalmos, although moderate in degree, was, as is the rule, an obtrusive symptom. The indications of exophthalmic goitre were most probably developed after the glycosuria had existed for an indefinite period of time, although being, as is usual, of insidious origin, it was impossible to fix the precise date of onset.

The Wassermann reaction gave a negative result. Two weeks prior to the fatal termination, bed-sores developed, and despite our best efforts to arrest them, became extensive and contributed to the gradually increasing exhaustion until the end was reached. During the twenty-four hours preceding death, coma, from which it was impossible to arouse the patient, developed. Death occurred on January 16, 1914. No autopsy was permitted.

Marinesco[5] reports a case showing, similarly, the association of acromegaly, diabetes mellitus, and certain unmistakable indications of Basedow's syndrome. Etiological significance in the production of hyperthyroidism has been attributed to acromegaly, but the nature of the relationship is not perfectly understood. Dock states that the diabetes arising in the course of acromegaly is cerebral and due to the pituitary disease, as shown by the fact that "diabetes is most marked with the largest tumors,"[4] an observation confirmed by our studies. According to Borchardt[6] this dictum is also corroborated by experiments on animals.

The metabolic changes caused by acromegaly are inconstant. Borchardt[6] in reports of 176 cases found diabetes recorded in 63 or 35.8 per cent., and alimentary glycosuria in 8 more. J. H. W.

Rhein[7] studied in the literature the symptomatology of 169 cases of tumor of the hypophysis and found glycosuria in only 7, or 4.1 per cent. Among these, 52 instances of acromegaly, or 30.8 per cent., occurred.

The purpose of the present statistical investigations has been to collect all of the cases of pituitary disease recorded in literature since the publication of the paper by Borchardt, or, in other words, a period of five years terminating December 31, 1913; also to either confirm or refute certain views which have been advanced in the past, notably that by Kollaritz,[8] that glycosuria does not

FIG. 1.—Showing hypertrophy of bones of face, characteristic of acromegaly.

FIG. 2.—Hypertrophy of bones of hand typical of acromegaly.

occur in tumors of the hypophysis without associated acromegaly. Again, it was hoped that the facts and data thus gleaned might aid in clearing up the question of the relation of hypo- and hyperthyroidism to acromegaly on the one hand and glycosuria on the other.

Our collective investigations yielded a total of 246 cases of hypophysial disease. In 183 cases the urinary findings were mentioned and showed 28 instances of glycosuria, in 9 of which the condition was intermittent, and the subjoined table represents an analysis of these cases.

Author.	Age and sex.	Lesions of pituitary.	Acromegaly.	Glycosuria.	Other ductless glands.	Remarks.
Cushing[16]	36 yrs. F.	?	Absent (hypopituitarism)	Glycosuria, intermittent Polyuria, constant	No mention	
Cushing[17]	40 yrs. M.	Tubercle of pars-anterior	Absent	Glycosuria, intermittent Polyuria constant	No mention	Glycosuria developed one year after operation.
Kocher[18]	30 yrs. F.	Sarcoma	Present	Diabetes, persistent	Thyroid, small Thymus, persistent	Patient operated upon.
Lucien and Parisot[19]	65 yrs. F.	Tuberculosis	Absent	200 to 300 gms. in 24 hrs.	.....	Pulmonary tuberculosis; pancreas normal.
Shoemaker[20]	35 yrs. F.	Adenocarcinoma	No mention	Glycosuria shortly before death	Thyroids and adrenals, normal	Bitemporal hemianopsia.
Messedaglia[21]	...	.....	Present	Glycosuria preceded hypophysial symptoms		
Church[22]	14 yrs. M.	Hemorrhagic cyst	Absent (infantilism)	Diabetes at 3½ yrs., duration not stated	No mention	Right temporal hemianopsia.
W. Romelaere[23]	...	Sarcoma	Present	Diabetes mellitus	Cirrhosis of pancreas and suprarenal glands	Blind. Death from bronchopneumonia.
Launois and Cleret[24]	33 yrs. F.	Sarcoma	Absent (hypopituitarism)	Diabetes mellitus	.....	Bilateral hemianopsia, mental torpor.
Moskalew[25]	52 yrs. F.	Epithelioma	Absent	1 to 4.5 per cent. sugar		
Foucault[26]	?	Tuberculosis	?	Diabetes mellitus	?	Thesis inaccessible.
Goldscheider[27]	51 yrs. F.	No tumor; assumes hypophysial alteration	Present	6 to 8 per cent. of sugar	Right ovary missing; thyroid and other ductless glands not mentioned	Glandular extracts had no effect. Exophthalmos present.
Marek[28]	26 yrs. F.	.....	Present	Began eighth month of pregnancy, disappeared after delivery	No mention	Primapara developed acromegaly late in pregnancy.
Echevarria[29]	...	?	Present	Diabetes mellitus	.....	Paper inaccessible.
Medigreceanu and Kristeller[30]	28 yrs. M.		Present	100 to 150 gms. per day; later increased tolerance		
Goetsch, Cushing and Jacobson[31]	...	.....	Present	Glycosuria, later increased tolerance		
Bittorf[32]	38 yrs. M.	Tumor (gumma?)	Present	Alimentary glycosuria	Thyroid normal	Binasal hemianopsia. Wassermann positive.
Amsler[33]	41 yrs. M.	Tumor	Present	Diabetes mellitus during acromegaly	Hyperplasia of spleen, pancreas and adrenals	Arteriosclerosis present.
Cushing[34]	32 yrs. M.	Gumma of pars-anterior and intermedia	Absent	Glycosuria disappeared; polyuria persisted	No mention	Slight exophthalmos.
Fisher[35]	29 yrs. M.	Fracture at base of skull	Absent	Glycosuria, intermittent first, 24 hrs. after fall	No mention	Glycosuria attributed to irritation of posterior lobe by extravasated blood.
Hill[36]	18 yrs. M.	Cyst	Absent (Frohlich's syndrome)	Marked polyuria. Glycosuria cleared after operation	Thyroid and thymus not palpable	Operation caused marked improvement. Attributed glycosuria to intracranial pressure.

Author.	Age and sex.	Lesions of pituitary.	Acromegaly.	Glycosuria.	Other ductless glands.	Remarks.
Carnot, Rathery and Dumont[8]	58 yrs. F.	Hypertrophy	Present	80 to 295 gms. in 24 hrs.	Thyroid sclerotic and cystic; suprarenals and pancreas sclerotic and hemorrhagic; ovaries sclerotic	
Fink[9]	...	?	Present	Diabetes mellitus	?	Dissertation inaccessible.
Sainton and Rol[10]	16 yrs. F.	Tumor probably malignant	Absent	Diabetes of grave juvenile type	Thyroid atrophied and sclerotic	Bilateral hemianopsia; knee-jerks exaggerated; speech slow.
Genella[6]	45 yrs. M.	Probable tumor	Present (atypical)	Glucose, 3 to 5 per cent.	.....	Difficulty in speech; reflexes diminished.
Meyer[11]	....	.....	Present	Diabetes mellitus	.....	Associated with paranoia.
Grinker[12]	49 yrs. M.	Adenoma	Present	Intermittent and slight	Thyroid not palpable	Subject to epileptic attacks.
Anders and Jameson	46 yrs. F.	Tumor	Present	Persistently present, 5 to 7 per cent.	Well-marked evidence of hyperthyroidism	Gangrene of hand. No hemianopsia.

It will be observed from a glance at the above table that 16 of the 28 cases of pituitary glycosuria, or 57.1 per cent., showed acromegaly, while 10, or 35.7 per cent. failed to show the latter condition in association. In 2 cases the presence of acromegaly was in doubt, hence excluded. It is interesting to note that of the 183 cases of pituitary disease in which the urinary findings were given, 88, or 42.6 per cent. showed acromegaly, and of the latter only 16, or 18.2 per cent. showed the presence of sugar. Moreover, it is a matter of no less interest that in 91 cases of pituitary disease in which acromegaly was absent, 10 showed spontaneous glycosuria, and no mention was made of either hypo- or hyperthyroidism in these cases.

The foregoing facts are not in accord with the observations of Kollaritz,[3] who recorded 52 cases of tumor of the hypophysis without acromegaly, of which not one was complicated by diabetes. Borchardt, writing in 1908, also affirms that since 1886 not one case of tumor without acromegaly was found in which glycosuria was associated. Sainton and Rol[10] state that although pituitary glycosuria without acromegaly may occur, it is rare. Here it is to be recollected that when spontaneous glycosuria is absent from this tripod of conditions, experimental observation may show the presence of an alimentary glycosuria. For example, Borchardt[11] reports 10 cases of acromegaly without spontaneous glycosuria, of which 8 showed the alimentary form, applying the usual test. He claims that glycosuria in one of its forms is more regularly present in acromegaly than in any other disease.

As an examination of the above table with reference to the character of the hypophysial lesions will show, there was tumor in

72 cases (of which 3 were specified as sarcoma, 2 as cyst, 1 adenocarcinoma, 1 epithelioma, 1 adenoma, and 4 as "tumor"), tuberculosis in 3, gumma in 2, hypertrophy in 1, fracture at base of skull with extravasated blood in 1, and lesion not stated in 8. The ages in our series were given in 21 cases, out of the total of 28, and found to average thirty-seven and one-quarter years, the period of life intervening between twenty-five and sixty years furnishing all save 3 cases.

In view of the fact that glycosuria not uncommonly complicates exophthalmic goitre, the question naturally arises whether in a case such as reported above it is to be attributed to the associated hyperthyroidism or to the hypophysial disease. As the result of the present investigations into the literature of the subject covering five years which ended January 1, 1914, there was but 1 case of hyperthyroidism in combination with pituitary lesions and glycosuria, out of a total of 28 cases recorded, namely, our own case herein reported, so that the role played by the thyroid gland in the causation of glycosuria in these cases would appear to be both trivial and obscure.

Cushing[12] states that in none of his 26 cases were there any symptomatic evidences of hyperthyroidism, but he found some degree of exophthalmos, which in all probability was a neighborhood effect of the tumor, to be common. On the other hand, Exner[13] refers to two of Hochenegg's patients with acromegaly and partial glandular extirpation, in which subsequent enlargement of the thyroid, occurred. It is highly probable that the results of various observers will not be in agreement on the point at issue for the reason that some of the cases are studied in the stage of insufficiency while others are investigated in that of hyperthyroidism. The balance of evidence—experimental, pathological, clinical—is in favor of the view that insufficiency of the thyroid gland increases carbohydrate tolerance. A. Lorand[14] believes that thyroidism is the dominating cause of the glycosuria in the rare cases in which pituitary disease and glycosuria coexist with Graves' disease.

Furnival found only 5 thyroids which could be considered normal out of 24 cases of acromegaly. Conversely, Schoneman's[15] studies of the pituitary body in 85 cases of goitre revealed marked alterations in all but one instance. In this connection two facts pointed out by Cushing are worthy of note: (1) that the two glands have some histological points of resemblance, and (2) that both have a somewhat similar influence on skeletal growth. Microscopic changes in the thyroid in cases of acromegaly are for the most part a low epithelium with excess of colloid.

As pointed out by Cushing, care must be exercised not to confuse mere exophthalmos due to neighborhood pressure with associated exophthalmic goitre. For example, there were 2 cases of simple

exophthalmos, the result of mechanical pressure, and only 1 of associated Graves' disease in our series of 28 cases.

In concluding, there are two hypotheses pertaining to the combined conditions discussed above which have received considerable corroborative support from our statistical inquiries: (1) that the relationship existing between hyperthyroidism and pituitary glycosuria, with or without acromegaly, is a remote one, and (2) that pituitary glycosuria without acromegaly not uncommonly occurs (in 10 of our series, as against 16 in which acromegaly was also associated) contrary to the opinions of certain writers.

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THE VALUE OF TESTS FOR RENAL FUNCTION IN EARLY AND ADVANCED BRIGHT'S DISEASE.[1]

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Since Richard Bright[2] described characteristic anatomical changes in various forms of kidney disease the problem of nephritis has occupied the attention of many observers. It is admitted that there are several types of nephritis, each one showing a different clinical course and different pathological lesions. It has been generally recognized that in the course of a nephritis, symptoms referable to toxemia have developed which have been given the inclusive name of "uremia," and that nephritic patients have died of uremia, of cardiac failure, or of some intercurrent cause. But it has been found impossible to predict in an individual case by clinical study alone what course the disease will take in its development or what anatomical changes will be found at autopsy. Therefore, during recent years, methods have been devised for estimating renal function in order to make possible an early diagnosis of existent kidney disease and to offer information in regard to its prognosis and treatment.

In 1881 Fleischer[3] followed the excretion of nitrogen, sodium chloride, and phosphoric acid in a series of nephritic cases. His patients were given a known diet, and were controlled by normal individuals with similar food. Fleischer found that the excretion of nitrogen in ratio to its intake in the pathological cases showed considerable variation, that phosphoric acid was poorly excreted, while the chloride balance was nearly perfect. These observations justify the assumption that in a diseased kidney, different parts show selective excretory functions tending to retain certain substances from the diet and to excrete others normally.

In 1910 Schlayer[4] and his co-workers began a series of experimental and clinical studies which have been of great value in the early diagnosis of abnormal renal function. Schlayer's original observations were based on acute experimental nephritis in rabbits. He injected potassium bichromate, cantharidin, or uranium nitrate into animals and produced a tubular, vascular, or mixed type of

[1] Read before the Section in Medicine of the New York Academy of Medicine, March 5, 1914.

[2] Guy's Hosp. Rep., 1836, i, 358.

[3] Deutsch. Arch. f. klin. Med., 1881, xxiv, 129.

[4] Schlayer and Takayasu, Deutsch. Arch. f. klin. Med., 1910, xcviii, 17; Ibid., 1911, ci, 333; Ibid., 1911, cii, 311; Verh. des. Cong. f. innere Med., 1912, xxix, 501; Beihefte zur med. Klin., 1912, ix, 211; Münch. med. Woch., 1913, lx, 800.

nephritis in which he studied renal function. He recognized the close relation which exists between renal blood-supply and the amount of urine excreted, and accordingly he studied general blood-pressure in his animals, changes in renal volume as recorded in an oncometer, and the diuretic response to various forms of stimuli, controlling the experiments by autopsy and histological examination. The various toxic substances produced different effects. In tubular nephritis Schlayer found that the renal vascular system reacted to vasodilators and constrictors normally. The urine, however, was dilute and the kidney was unable to concentrate and excrete sodium chloride when it was injected intravenously. In vascular nephritis, on the other hand, the kidney's concentrative powers were unaffected while the vascular response to vasomotor stimuli was lost or exaggerated. This led him to determine whether the excretion of other substances in addition to that of chloride might be used as a measure of the efficiency of the vascular or tubular apparatus of the kidney to replace observations with the oncometer. One of the prominent features of his experiments was the amount of fluid excreted. In tubular nephritis it was not remarkable; but in vascular nephritis it varied directly with the vascular functional condition. In cases where the renal vessels were hypersensitive to vasodilators there resulted a diuresis; when the vessels were insensitive there was oliguria. Thus the amount of urine obtained was one index to glomerular function. Voit[5] discovered that if lactose was injected into an animal intravenously or subcutaneously the entire amount could be recovered in the urine. Schlayer, however, found in experimental nephritis that intravenous injections of this sugar were only well excreted when the renal vascular system was normal, and were held back when the glomeruli were damaged. Therefore he assumed that lactose in addition to water might be used as a test for the vascular condition of the kidney. Schlayer recognized the complexity of chloride metabolism. Duckworth[6] had already introduced potassium iodide as a test for renal function, and Schlayer, comparing its excretion with that of sodium chloride, found that both were distinctly interfered with in tubular lesions. So Schlayer adopted the excretion of water and lactose as indicators of renal vascular activity, and that of sodium chloride and potassium iodide as measures of tubular activity. Experimentally there was a close agreement between the excretion of these substances and the respective types of nephritis, which confirmed Schlayer's views as to their place of excretion.

He turned these methods to the study of patients. His technique for the various tests was simple. While under observation

[5] Deutsch. Arch. f. klin. Med., 1897, lviii, 545.
[6] Saint Bartholomew's Hosp. Rep., 1867, iii, 216.

the patient was ordered a constant diet containing known amounts of fluid and salt. The total amount of fluid and sodium chloride excreted was followed from day to day. To make the lactose test 2 gm. of the sugar dissolved in 20 c.c. of distilled water were injected intravenously. After the injection the urine was collected at the end of four hours and every hour or two thereafter to twelve hours. Each specimen was tested for the presence of sugar with Nylander's reagent, and the total amount of sugar excreted was determined polarimetrically. Normally 60 per cent. or more of the amount injected was regained in from four to six hours.

On a certain day the patient was given 10 gm. of salt by mouth. Normally this should be excreted in from twenty-four to forty-eight hours, either by an increase of salt concentration in the urine or by diuresis. Schlayer found, however, that there were two types of abnormal salt excretion. In experimental tubular nephritis, with intact glomeruli, the kidney could not concentrate chloride and the salt was retained in the body. The specific gravity of the urine was low, and to this type of dilute urine Schlayer gave the name "tubular" hyposthenuria. The other type of abnormal chloride excretion occurred in experimental nephritis, where the tubules were normal but where the vessels were hypersensitive to stimulation. As a result the diuretic action of the salt was marked, and the added salt was excreted in an excess of fluid, its concentration remaining low and the specific gravity of the urine remaining unchanged. Schlayer called such a dilute urine "vascular" hyposthenuria. Both types of chloride excretion were found to occur clinically.

The length of time required by the kidney to excrete 500 mg. of potassium iodide given by mouth served as a criterion for the iodide test. Janeway[7] has pointed out that this depends upon the qualitative reaction which is used to determine the presence of iodine in the urine. Schlayer selected Sandow's test and considered sixty hours normal, while von Monakow,[8] taking starch paste and nitric acid, made forty-four hours the upper limit.

By using these various tests, Schlayer claims to be able to distinguish certain types of acute and chronic nephritis and to find their distinguishing characteristics to be sharply demarcated. Vascular nephritis, whether acute or chronic, is characterized by a delayed lactose excretion, by oliguria or polyuria, depending on the sensitiveness of the renal vessels, and by a normal chloride and iodide excretion. Tubular nephritis is shown by a normal water and lactose excretion, but with delayed chloride and iodide outputs. All grades of mixed functional disturbances are found between these two extremes. In a general way the tests point out

[7] Trans. Cong. Amer. Phys. and Surg., 1913, ix, 14.
[8] Deutsch. Arch. f. klin. Med., 1911, cii, 248.

the severity of the disease, and since they are all delicate, often show functional changes before clinical signs of nephritis develop. Schlayer has shown this prettily by observing cases over a long interval of time. He has been able to see cases with abnormal function by the tests later develop albuminuria, cylindruria, and hypertension. Repetition of the tests in such cases has demonstrated a progressively worse renal function with the increasing clinical severity of the disease. The work of Conzen,[9] Eppinger and Barrenscheen,[10] Rowntree and Fitz,[11] Herringham and Trevan,[12] Eisner,[13] Michaud and Schlecht,[14] and Frank and Benrenroth[15] confirms the value of Schlayer's methods in the diagnosis of nephritis.

In regard to the anatomical changes producing the functional disturbances, however, there is a difference of opinion. Von Monakow found a delayed potassium iodide excretion when the salt excretion was undisturbed, and believed that disturbance of water excretion depended on tubular degeneration. Rowntree and Fitz considered lactose an index of the vascular condition of the kidney, but showed in the frog at least that the tubules in the absence of a glomerular system were capable of excreting the sugar. In summing up the relation of functional tests to pathological diagnosis in nephritis, Christian[16] states that "so far too few cases are recorded with these functional tests and subsequent histological examination of the kidneys to justify final conclusions, but such as are recorded do not seem to indicate that any very close correlation between function and anatomical lesion can be made on the basis of the rate of excretion of such substances as lactose, potassium iodide, salt, and water."

Von Monakow, repeating Schlayer's work, added a nitrogen test to the others. This consisted in following the nitrogen balance during the period of observation, and on one day giving 20 gm. of urea, containing 9.3 gm. of nitrogen. According to his observations it was normally excreted within forty-eight hours, but was retained in nephritides with glomerular lesions. Although subsequent work has not proved the place of its excretion, there seems little doubt at present that the kidney has selective excretory capacities. The excretion of lactose, water, and nitrogen differs from that of sodium chloride and potassium iodide. By following the excretion of these substances and by adding test amounts it is possible to discover an abnormal renal function before marked clinical signs of kidney disease are manifest. The different types

[9] Deutsch. Arch. f. klin. Med., 1912, cviii, 353.
[10] Wien. med. Woch., 1912, lxii, 1408, 1497.
[11] Arch. Int. Med., 1913, xi, 121; ibid., 258.
[12] Quart. Jour. Med., 1913, vi, 505.
[13] Deutsch. Arch. f. klin. Med., 1913, cxii, 442.
[14] Jahreskurse, f. ärtzl. Fortbildung, 1913, iv, 3.
[15] Verh. des Cong. f. innere Med., 1913, xxx, 217.
[16] Trans. Cong. Amer. Phys. and Surg., 1913, ix, 1.

of functional disturbance are well illustrated by the following cases:

CASE I.—Tubular nephritis. Peter Bent Brigham Hospital. Medical No. 782.

A man, aged forty years, came to the hospital with acute articular rheumatism. His history was unimportant except for a previous attack of rheumatic fever. Three months ago he became unconscious while at work, remaining in this condition for four days. No paralysis was noted at the time. He made a normal recovery.

At entry, physical examination showed an enlarged heart. There was a faint systolic murmur at the apex. The aortic second sound was accentuated. The systolic blood-pressure was 185. There was moderate thickening of the peripheral vessels, and the urine showed a trace of albumin with occasional casts. The fundi oculorum were normal. There was no edema.

At the time the tests for renal function were made the acute stage of rheumatic fever had passed. The results of the functional tests are charted below.[17]

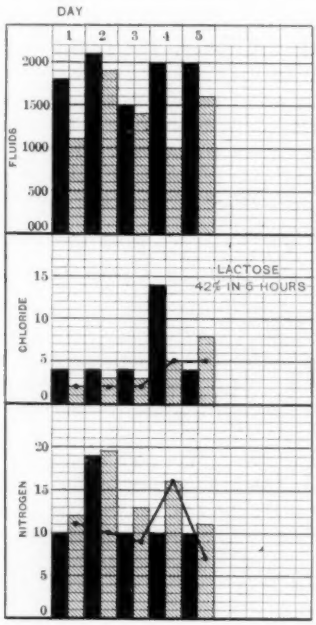

CHART I.—"Tubular" nephritis.

[17] The black column in the accompanying charts represents intake, the cross-column output, the dotted lines the concentration of chloride or nitrogen per 100 c.c. of urine.

While the functional findings are not absolutely typical the striking feature is retention of chloride and water when added salt was given, while added nitrogen is excreted normally. This suggests tubular involvement. On the other hand the lactose excretion is somewhat delayed, and therefore vascular function must be interfered with to a certain extent. The case is called "tubular" because it illustrates with more than usual distinctness the type of excretion which characterizes abnormal tubular function.

Case II.—Vascular nephritis. Peter Bent Brigham Hospital. Medical No. 131.

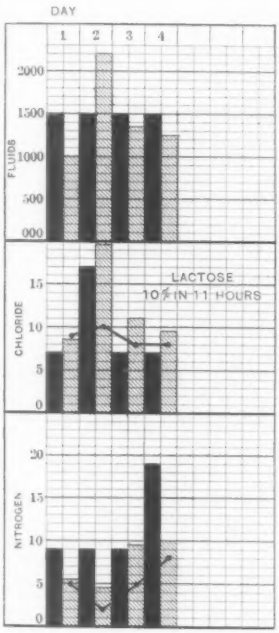

Chart II.—"Vascular" nephritis.

A woman, aged thirty years, entered the hospital complaining of "shortness of breath." As a girl she had scarlet fever and "convulsions." Ten years ago she noted shortness of breath on exertion. Two years ago her face and eyes were swollen at times. During the past year her physician had observed a high blood-pressure. On two or three occasions during this time she had mild convulsions, from which she recovered quickly. There was more or less headache.

Physical examination showed marked cardiac hypertrophy. There was a systolic murmur at the apex, and another of different pitch and intensity at the base. The aortic second sound was accentuated. The systolic blood-pressure was 200. The urine showed albumin and casts. The specific gravity was between 1010 to 1015. Fundus examination showed edema and hemorrhage of the disks without exudate.

In this case the vascular system was especially at fault. The lactose and nitrogen were poorly excreted. The tubules were able to increase the concentration of chloride, but the salt acted mainly as a diuretic, increasing the urinary output markedly. Thus the vessels were hypersensitive and as the specific gravity showed a relative fixation during the period of observation, the functional findings are those of "vascular hyposthenuria."

CASE III.—Mixed nephritis. Peter Bent Brigham Hospital. Medical No. 75.

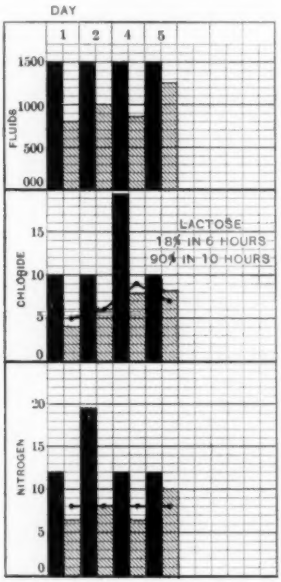

CHART III.—"Mixed" nephritis.

A painter, aged forty-five years, came to the hospital complaining of weakness of the arms and legs. His previous and family histories were negative. Physical examination gave signs of a peripheral neuritis, probably due to lead poisoning. In addition his heart was slightly enlarged, the aortic second sound was ringing, the

blood-pressure was 160, and the urine was of a fixed gravity, between 1014 to 1015, and contained albumin and casts. His renal functions were studied with the results shown above.

Here the function of both the tubules and vascular system was involved. There was a delayed lactose and nitrogen excretion; the vessels were insensitive to chloride stimulation. Salt concentration increased slightly, following the added amount, but not enough to increase the total output. Thus a mixed type of functional derangement was found, without a typical "vascular" or "tubular" hyposthenuria.

On the whole, Schlayer's tests are significant, chiefly because they show early functional disturbances in the kidney, and by repetition illustrate the rapidity of development of an early disease. But whether vascular and tubular function on an anatomical basis can be differentiated in Bright's disease with the same definition as in experimental toxic nephritis, remains to be determined by a careful study of more clinical and pathological material.

In advanced nephritis these tests are less useful. In the first place it is difficult to conceive of such a kidney in which pathological and functional lesions are not found in both tubules and vascular system to so great a degree as to make differentiation of function impossible. In the second place, whatever disturbances are found may be identical with those occurring in an early disease, and so give little prognostic information. The latter point is well demonstrated by the cases quoted. The most advanced case to all clinical appearances was the one recorded as "vascular" nephritis. Yet by the tests the worst case functionally was the one which showed the "mixed" type of excretion, and occurred in a man who had no symptoms of kidney disease whatever. Therefore in advanced Bright's disease, tests which estimate the total renal function and which are directed to determining the cause of symptoms encountered are of more value than finer ones which attempt to study individual functions of different anatomical units of the organ.

It is generally agreed that the kidney is the main excretory channel of the body, and that retention of substances through faulty elimination may lead to toxic manifestations. Prevost and Dumas,[18] in 1821, found an increase in the urea content of the blood after extirpation of the kidneys. From that time various observers have isolated specific substances from the blood of uremic patients which they have considered the cause of symptoms. But each body successively incriminated has been successively rejected. At present renal insufficiency or uremia is regarded as a complex intoxication arising from unknown causes. But the degree of renal insufficiency can be estimated in a variety of ways.

[18] Quoted by Schöndorff, Pflüger's Arch. f. d. ges. Phys., 1899, lxxiv, 307.

In phenolsulphonephthalein, Rowntree and Geraghty[19] have given the most valuable single aid to the estimation of total renal function, which is known at present. Phenolsulphonephthalein is a dye devoid of toxicity, and is eliminated from the body almost entirely through the kidney. Rowntree and Geraghty have shown from careful studies in nephritis that the amount of phthalein excreted varies in direct proportion to the severity of the disease. In fatal uremia only traces of the dye are found in the urine, while in mild nephritis the amount recovered is nearly normal. In cardio-renal disease where the heart is chiefly at fault and the kidneys are congested without a marked nephritis a low phthalein output may be observed at first, rapidly rising as the circulation is restored, while if a severe nephritis is present no change in the phthalein excretion accompanies the improved circulation.

In addition to its accuracy the test has the added advantages of being rapid and so simple that it may be used by the general practitioner. A solution of phenolsulphonephthalein is made containing 6 mg. of the dye to 1 c.c. of salt solution. This is injected either intravenously or intramuscularly under aseptic conditions. Following the injection all the urine excreted is collected at the end of one hour and two hours, is diluted to a suitable amount with alkaline water, and its phthalein content is estimated by colorimetry. The Du Bosc q colorimeter may be used or the simpler Autenrieth-Königsberger machine or even a series of test-tubes containing varying amounts of the dye in varying dilutions. If the colorimeter is used a standard solution for comparison is made which contains 6 mg. of phthalein in a liter of alkaline water. Normally from 40 to 60 per cent. of the amount injected is recovered in one hour, and from 60 to 80 per cent. in two hours following intramuscular injection. The test has been used successfully by so many observers that its value must be accepted as a fact.

In a few cases, however, the excretion of the dye gives unreliable information. This appears to be because a diseased kidney may be hyperpermeable to one substance, while it is impermeable to another. Thus it may be permeable to a dye and impermeable, possibly, to an unknown poison causing certain symptoms of the disease. Bard and Bonnet,[20] in studies on renal function in which potassium iodide and methylene blue were used as tests, found that in interstitial nephritis the excretion of both substances was faulty, in "epithelial" nephritis the kidney was hyperpermeable for both, and in secondary interstitial nephritis the methylene-blue excretion was normal or increased, while that of potassium iodide was diminished. Pepper and Austin[21] have lately called attention to a case of nephritis with marked albuminuria, cylindruria, and

[19] Jour. Pharm. and Exp. Ther., 1909, i, 579; Arch. Int. Med., 1912, ix, 284.
[20] Arch. Gén. de Méd., 1898, 3d ser., ix, 129, 283, 464.
[21] AMER. JOUR. MED. SCI., 1913, cxlv, 254.

edema in which the phthalein output was normal, and Baetjer[22] reports nearly similar cases. Foster[23] illustrates the difficulty of prognosis by the use of any one kind of functional test giving as examples cases which died of uremia with a practically normal phthalein output shortly before death. In this regard the following case is of interest.

CASE IV.—Peter Bent Brigham Hospital. Medical No. 4.

A woman, aged sixty-three years, was admitted to the hospital with a history of dyspnea of one year's duration. Her family and previous histories were negative. Her habits were good. Two months before entry her eyesight had failed, and she began to have mild occipital headaches. Physical examination was unimportant except for marked cardiac hypertrophy, an apical systolic murmur, an increased blood-pressure (232 mm. systolic), and a urine which contained albumin and casts. She appeared to be a case of advanced interstitial nephritis, confirmed by a phthalein excretion of 12 per cent. for two hours. Rest in bed produced no benefit. In two weeks she became drowsy and was bled. On the following day the phthalein excretion was 30 per cent. for one hour and twenty minutes. Her general condition did not improve. A week later she became comatose and put out only traces of phthalein in two hours. She was bled again. She became brighter temporarily, and her phthalein excretion on the next day was 54 per cent. for two hours. She lapsed into coma soon and died shortly. On the day of her death she put out 8 per cent. of phthalein in two hours. Autopsy showed typical contracted kidneys. It is difficult to explain this rapid premortal rise in the excretion of phthalein on any other ground than that bleeding had in some way rendered the kidney hyperpermeable to the dye without having any definite influence on the disease.

But, on the whole, the phthalein test is of great value. These latter observations merely emphasize that to judge the degree of renal insufficiency with accuracy more than one test must be used.

Of substances studied in the blood of nephritics the concentration of the incoagulable nitrogen and urea has been found to be of most importance. Folin and Denis[24] and Marshall[25] have recently devised relatively simple methods for performing these analyses, making possible such estimations as a matter of routine in hospitals with well-equipped laboratories. In regard to the technique employed, readers are referred to the original articles. The older methods required large amounts of blood, and were time-consuming. Nevertheless, Ascoli,[26] Strauss,[27] and others found in severe grades

[22] Arch. Int. Med., 1913, xi, 593.
[23] Arch. Int. Med., 1913, xii, 452.
[24] Jour. Biol. Chem., 1912, xi, 527.
[25] Ibid., 1913, xv, 487.
[26] Pflüger's Arch. f. d. ges. Phys., 1901, lxxxvii, 103.
[27] Die Chronische Nierentzündungen in ihrer Einwirkung auf die Blutflüssigkeit und deren Behandlung, Berlin, 1902, A. Hirschwald.

of nephritis the nitrogen usually though not invariably increased, the increase being much more marked toward death. Obermayer and Popper[28] showed that cases of uremia have a higher incoagulable nitrogen content in the blood than do normal individuals or cases of nephritis without uremia, and that of this nitrogen the urea fraction increases with the development of intoxication. Widal[29] has gone so far as to believe that it is possible to base an approximate prognosis as to length of life on the degree of urea retention.

Opposed to this, Strauss,[30] in a recent paper, describes different clinical types of uremia, and says that high values for blood-nitrogen are usually accompanied by uremic manifestations, but that a low concentration for nitrogen does not mean a favorable outcome for the disease, because fatal uremia may develop when low figures are present as well as when high figures are found. Foster's results bear out this statement. Thus this test is not infallible, and proves again that to judge accurately the degree of renal insufficiency more than one test for renal function must be made.

The relation of faulty sodium chloride excretion to edema in nephritis and its independence of nitrogen retention has been proved by Widal,[31] although Bickel[32] in a series of analyses was unable to find any relationship between the development of uremia and the amount of chloride accumulation in the blood as estimated by electrical conductivity. The apparent contradiction of faulty chloride elimination without an increase of its blood-concentration has been explained by two hypotheses. Bohne,[33] by determining the chloride content of nephritic organs at autopsy in a limited number of cases, believed that the salt was stored in the tissues rather than in the blood, while Marie[34] has assumed that in nephritis chlorides are retained in a "free" state where they increase the concentration of the blood and tissues, and in this way produce accumulation of fluid or circulate as a "fixed" compound when they are inactive. Whatever the relation of salt retention to edema may be, there is no doubt that certain cases of advanced nephritis with normal function in other regards are unable to excrete sodium chloride and develop edema. The cases reported by Austin and Pepper and by Baetjer show this strikingly. In Baetjer's cases, which were of well-marked nephritis, the phthalein and lactose outputs were normal or increased; yet the patients were unable to excrete chloride, and after its administration retained water. Apparently Austin and Pepper's case is of the same type. This

[28] Ztsch. f. klin. Med., 1909. lxvii, 332.
[29] Bull. et mém. d. hôp. de Paris, 1911, series 3, xxxii, 627.
[30] Deutsch. Arch. f. klin. Med., 1912, cvi, 219.
[31] Verh. des. Cong. f. innere Med., 1909, xxvi, 43.
[32] Deutsch. med. Woch., 1902, xxviii, 501.
[33] Fortschr. der Med., 1897, xv, 121.
[34] Sem. Méd., 1903, xxiii, 385.

shows from another point of view that more than one kind of test must be made to estimate the total renal function.

Finally, there is considerable evidence at hand that certain manifestations of renal insufficiency are produced by the retention of acids in the body, with a consequent acidosis. This can be measured by direct determination of blood-alkalinity, by following the carbon dioxide tension of expired air, since it has been shown to be diminished in various acidoses, or by determining the urinary acidity. Older methods for determining blood-reaction based upon its direct titration against normal acids are inaccurate. Nevertheless, von Jaksch,[35] in 1888, found the reaction of the blood abnormally acid in uremia, and this was confirmed by Peiper[36] and Orlowski.[37] Brandenburg[38] compared the nitrogen of the blood with its reaction in a variety of cases, and made the interesting observation that in uremia there was often an acidosis which bore no relation to the degree of nitrogen retention. While these observations are not beyond criticism, the recent work of Straub and Schlayer,[39] and of Porges and Leimdörfer[40] proves that the results obtained are important. Working with Haldane's instrument, these observers have noted independently a lowering of the carbon dioxide tension in uremic cases, concluding that the condition has to do with acidosis. Sellards,[41] Palmer,[42] and Palmer and Henderson[43] have considered an increased urinary acidity as another sign of acidosis, and have found it a frequent occurrence in nephritis.

All these observations show that the study of renal function in advanced nephritis is extremely complex. A diseased kidney affords as varied a picture in regard to its functional diagnosis as it does in regard to its clinical manifestations. None of the tests, alone, which have been considered, justify a definite estimate of the renal function in every case, nor has their relationship to each other and to the clinical and pathological condition associated with them been controlled in a sufficient number of cases to establish their real meanings. There is no doubt, however, that a variety of tests for renal function helps to make a diagnosis of kidney disease before definite signs of nephritis manifest themselves, and affords accurate information in regard to prognosis by estimating the degree and type of renal insufficiency. Moreover, a series of such tests is of help in treatment.

Widal[44] believes that three distinct symptom complexes occur

[35] Ztschr. f. klin. Med., 1888, xiii, 350.
[36] Virchows Arch., 1889, cxvi, 337.
[37] Cent. f. Stoffw. v. verd. Krankh., 1902, iii, 123.
[38] Ztschr. f. klin. Med., 1899, xxxvi, 267.
[39] Münch. med. Woch., 1912, lix, 568.
[40] Ztsch. f. klin. Med., 1913, lxxvii, 464.
[41] Johns Hopkins Hosp. Bull., 1912, xxiii, 289.
[42] Boston Med. and Surg. Jour., 1913, clxix, 464.
[43] Jour. Biol. Chem., 1913, xiii, 393; Arch. Int. Med., 1913, xii, 146.
[44] Le Mouvement Médical, 1913, i, 1.

in cardiorenal disease. Patients with high blood-pressure suffer from one train of symptoms which include circulatory disturbances, like tinnitus, vertigo, headache, cerebral hemorrhage, or cardiac decompensation. Patients with chloride retention suffer from equally characteristic symptoms. Here edema is the underlying factor. The digestive, nervous, or respiratory organs may be affected, depending on the situation of the edema, with diarrhea, delirium and convulsions, or dyspnea. Patients with nitrogen retention do not develop edema, but show albuminuric retinitis, a progressive loss of appetite, anemia, and coma. Such individuals are subject to ulcerative gastro-enteritis, pleuritis, or pericarditis. Naturally the symptoms become intermixed in advanced cases, so that a sharp division is impossible. But Widal considers that in the "hypertensive" cases the heart must be watched, in the chloride retention cases with edema, a salt-poor diet is indicated, and that the nitrogen retention cases are the most severe and hopeless.

Such a dogmatic division of symptoms in cardiorenal disease needs confirmation. But a rational diet based upon the kidney's selective excretory capacity can be instituted by following the excretion and blood-concentration of nitrogen, salt and water. Von Noorden[45] has formulated general rules for the protective treatment of nephritis. A case can be treated on a less empirical basis, and more as an individual by making these simple tests. It is fair to assume that cases unable to excrete chloride should be given a salt-poor diet; cases unable to excrete nitrogen and with nitrogen accumulation in the blood should be given low protein diets, and cases of acidosis with normal functions in other respects should receive alkalies.

For these reasons, tests for renal function in Bright's disease are important for diagnosis, prognosis, and treatment. The lactose, salt, water, potassium iodide, and nitrogen tests are of special value in the early diagnosis of nephritis. In advanced nephritis the functional condition is so complex that tests to estimate total function are more useful than those designed to study the function of different parts of the kidney. The phthalein excretion is the most satisfactory single test. The non-protein nitrogen of the blood offers additional information in regard to faulty eliminative powers on the part of the kidney. Yet cases occur in which both blood-nitrogen and phthalein are normal, and chloride retention is an important factor in the disease. Finally, acidosis has been shown to exist in uremia. Since no one test is perfect in determining total renal function, cases must be studied from several points of view. A rational dietetic treatment can be given in individual cases based on the conditions disclosed by the study of the kidney's selective excretory capacity.

[45] Metabolism and Practical Medicine, Chicago, 1907, ii, 47[illegible]

OBSERVATIONS ON THE INTRAVENOUS USE OF STROPHANTHIN WITH REGULAR AND IRREGULAR PULSE RHYTHMS.

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Since Fraenkel,[1] in 1906, reported the value of intravenous injections of strophanthin in heart failure—noting increased amplitude and slowing of the pulse, together with diuresis—observations on the intravenous use of this drug with favorable results have followed in considerable numbers from other writers. However, these observations have not been explicit as to the type of cases in which strophanthin was employed, and until the more recent reports of Agassiz[2] and Linnell,[3] have produced the impression that it yielded beneficial results in all cases of heart failure, regardless of the pulse rhythms. This is clearly not so, and the type of cases in which good results are obtained is so sharply defined that it would seem to deserve more emphasis than it has generally received.

The present report is made with the object of studying further the nature and duration of the actions of strophanthin in cardiac lesions, with particular reference to the pulse rhythm present, since this feature decides how effectual the injections will prove. The work of Mackenzie[4] has made clear that digitalis and its allies produce their striking results in a clearly marked group of clinical cases. Definite slowing of the pulse under digitalis occurs in the presence of the pulsus irregularis perpetuus and the ventricular form of venous pulse, the complex familiar as auricular fibrillation. In conditions other than auricular fibrillation it produces also at times a slowing of the pulse that is more apparent than real and occasionally to the disadvantage of the patient. It is a matter of record that digitalis administration in the presence of a normal regular pulse rhythm may produce for the time being, and sometimes permanently, any of the commoner irregularities of the heart, such as premature contractions, phasic variations, heart-block, pulsus alternans, and auricular fibrillations (Fig. 1). Frequently, too, the finger is taken as a guide to the slowing of the pulse in these instances, and may readily lead to erroneous conclusions, since an apparently long interval between pulse waves may be due to a weak contraction perceptible at the

[1] Fraenkel, Verhand. d. Kongress f. innere Medizin, 1906, xxiii, 257.

[2] Agassiz, C. D. S., Observations on the Effect of Strophanthin in Cases of Auricular Fibrillation, Heart, vol. iii, No. 4, p. 353.

[3] Linnell, J. W., The Use of Strophanthin Administered Intravenously in Cases of Heart Disease. Publication printed for private circulation, London, 1913.

[4] Mackenzie, James, Digitalis, Heart, vol. ii, No. 4.

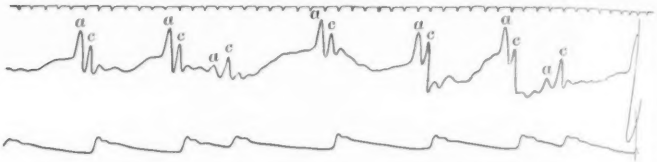

FIG. 1 (*a*).—Marked sinus arrhythmia induced by digitalis in a previously regular pulse.

FIG. 1 (*b*).—Heart block occasioned in a previously regular pulse by digitalis (septic endocarditis).

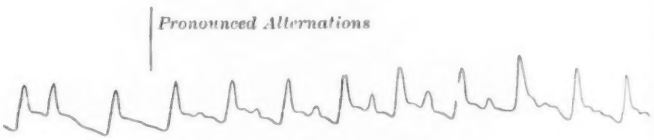

FIG. 1 (*c*).—Pulsus alternans.

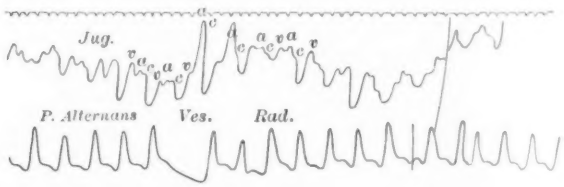

FIG. 1 (*d*).—Ventricular extrasystole induced in a previously regular pulse after a total administration of ℥iij tinct. strophanthus.

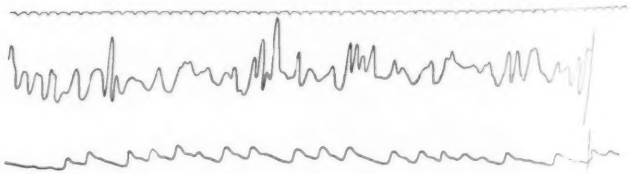

FIG. 1 (*e*).—Auricular fibrillation (permanent) induced after ℳxxx tinct. digitalis. Case of Dr. J. D. Heard.

FIG. 1.—Illustrating irregularities brought on in previously regular pulse rhythms by the administration of digitalis and strophanthus. Time marked in all cases in one-fifth second.

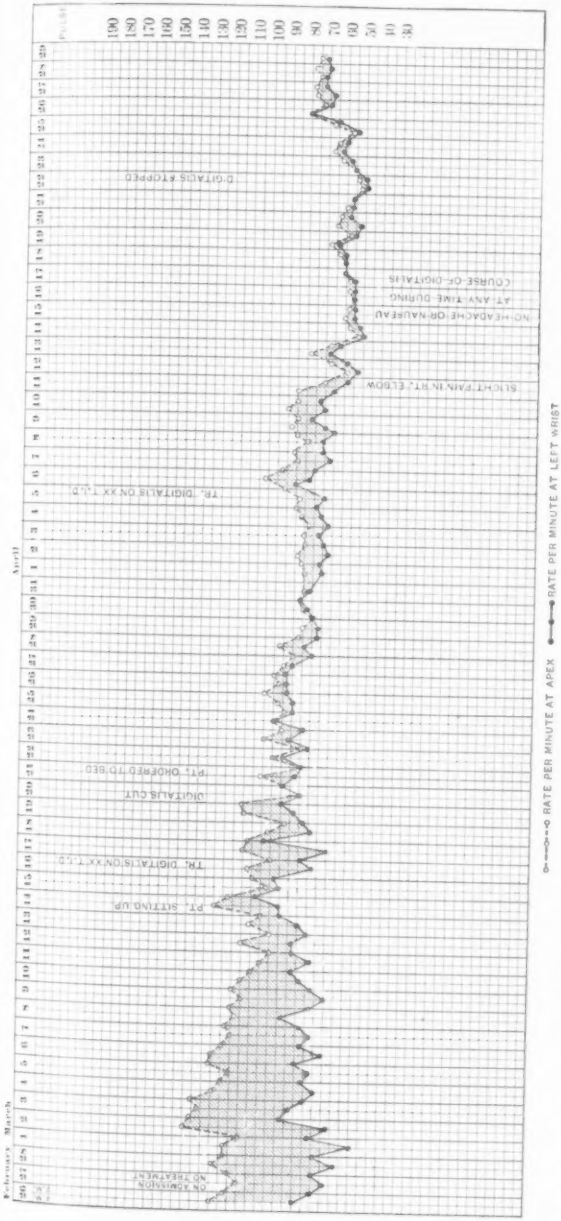

FIG. 2.—Showing diminution of pulse deficit after digitalis administration in auricular fibrillation. Upper level, apex rate. Lower level, pulse at wrist.

apex but too feeble to reach the wrist. The same holds true to even a greater degree in auricular fibrillation, as is commonly attested by most clinical charts, the pulse rate as recorded by the nurse being many counts below the actual heart beat. This difference in rate between apex and radial pulse—the pulse deficit—may, as pointed out by James and Hart,[5] be made a guide to the patient's improvement, since it progressively grows less or even disappears under treatment (Fig. 2).

In the present observations the pulse has been termed irregular in the presence of a disorderly rhythm with no two beats alike in length or amplitude, and a positive venous pulse, and regular if there is evidence of an underlying, orderly arrangement of contractions, even though these be interrupted by contractions of atypical origin. In all, twenty cases with regular and irregular pulse rhythms were studied. Those having regular rhythms were all clearly definied, and showed no intercurrent irregularities.

Preparations Used and Dosage. Two forms of strophanthin were used, and, so far as could be judged, showed no difference in efficiency—the ampoules of Boehringer containing 1 mg. each, or $\frac{1}{60}$ gr., and the tablets of Burroughs, Wellcome & Co., of $\frac{1}{75}$ gr. each, dissolved in sterile water. As a rule $\frac{1}{60}$ gr. was employed. A dose of less than $\frac{1}{120}$ gr. did not prove practicable, and, except in one instance that will be mentioned, we saw no ill effects from $\frac{1}{60}$ gr. The smaller the dose the more frequently it may be employed, but since the procedure is not a painless one, it seemed always desirable to give at one time the largest dose within the limits of safety. A dose of $\frac{1}{60}$ gr. should, and need, scarcely be repeated in less than forty-eight hours.

The injection was made with a hypodermic syringe into a vein at the bend of the elbow, the arm having been surgically cleansed and a tourniquet applied. It is important after introducing the needle, and before pressing the plunger, to see that blood is flowing into the syringe so as to make sure that none of the injection enters the subcutaneous tissues and causes a cellulitis. In two cases a red, swollen, tender arm resulted from some of the strophanthin escaping into the subcutaneous tissues, the symptoms subsiding after three or four days. One case, already *in extremis*, had her death hastened by what must have been too great a dose for her body weight. Otherwise, no ill effects were noted, such as rigors, headaches, and rises of temperature, which some observers have reported.

Effect on the Heart Rate and its Duration. In those cases which reacted, slowing of the pulse rate occurred within twenty minutes, though in some instances a maximal effect was not obtained for six to eight hours. Where a sufficient dose was

[5] James and Hart, Auricular Fibrillation, Clinical Observations on Pulse Deficit, Digitalis, and Blood-pressure, Amer. Jour. Med. Sci., January, 1911, p. 63.

injected to obtain a maximal slowing, the pulse did not begin to accelerate again for three to ten days. The duration of the effect seemed to be proportionate to the extent of slowing rather than to the dosage employed, as already noted by Agassiz.[6]

Other Effects. Where the subjective symptoms are urgent, the effect of strophanthin in suitable cases is most striking. Coughing and dyspnea cease within a few minutes, and the patient experiences a relief comparable in its rapidity only to that obtained from morphine, while the heart rate is sufficiently lowered to tide him over until digitalis, administered orally, can produce its effects. On the other hand, it was interesting to observe that an enlarged pulsating liver did not at once diminish in size, but retreated only after a number of days to its normal dimensions. Similarly, we could not observe any reductions in the heart outlines, either immediately or subsequently. Blood-pressure also was little affected, but showed a tendency to a moderate rise whenever decisive slowing occurred. The cases which reacted decisively did not, except in one instance, revert to a regular rhythm, but continued to fibrillate at a lower rate.

Cases Studied. Of the 20 cases in this series, 10 showed the pulsus irregularis; in 9 of these it was constant, in 1 it interrupted the normal rhythm in paroxysms; 10 cases had at all times a regular, rapid pulse, 9 of these being an acceleration of the normal pacemaker rhythm; 1 being a case of paroxysmal tachycardia of auricular origin.

With one exception all the cases studied showed a valvular lesion, with accelerated pulse. In the one exception there was pulse acceleration without cardiac lesion in a postoperative laparotomy, terminating fatally.

Of the cases with pulsus irregularis, 6 had a rapid pulse (in all cases over 100) and slight dyspnea, but no further symptoms. The other 4 were seriously ill. The reaction in all cases was decisive, the pulse rate dropping from 20 to 60 beats per minute, the maximum of reaction being reached in twenty minutes to eight hours. In one instance, where three doses of $\frac{1}{120}$ gr. were given during a week, the maximal reaction did not occur until one hour after the final injection (Fig. 3).

Of the 4 serious cases, 1 on the service of Dr. James D. Heard, at St. Francis' Hospital, afforded very striking results. This case has been reported in detail.[7] It will suffice to say that from a condition of extreme dyspnea with a totally irregular apex beat of 164, pulmonary congestion, enlarged pulsating liver, and great edema of the lower extremities, the patient was brought in twenty minutes after the injection of $\frac{1}{120}$ gr. to a condition of

[6] Loc. cit.

[7] Cohn, A. E., and Heard, James D., A Case of Auricular Fibrillation with Post-mortem Examination, Archives of Internal Medicine, June, 1913.

comfort, with an apex beat of 116. Four hours later a second injection of $\frac{1}{120}$ gr. was given, bringing the pulse to 100, after which the oral administration of digitalis was begun.

Two instances of pulsus irregularis occurred in association with pneumonia. In both instances the irregularity antedated the pneumonia—in the first by ten years and in the second by three. There was a severe toxemia. In the first case $\frac{1}{120}$ gr. of strophanthin reduced a pulse of 160 to 80 in one hour. In the second case the same dose caused a drop from 144 to 92 in the same time. Notwithstanding the strikingly favorable results as to the cardiac mechanism, both cases pursued their unfavorable course to a fatal termination.

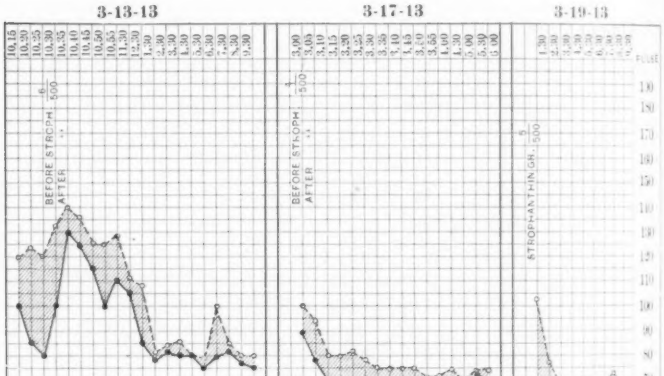

FIG. 3.—Showing progressive lowering of apex rate and pulse deficit by repeated injections of strophanthin.

The last case with occasional pulsus irregularis occurred on the service of Dr. R. T. Miller, Jr., at St. Francis' Hospital, where he had been admitted for a gall-stone operation. One paroxysm of pulsus irregularis occurred before operation, but terminated spontaneously. Two others occurred after operation, with an apex rate of 140 and great distress. In each postoperative instance the normal rhythm, at a rate of 76, was resumed within one-half hour after administering $\frac{1}{120}$ gr. strophanthin. However, it is difficult to say how far these injections were responsible for any improvement in view of the spontaneous termination of the first attack.

CASES PRESENTING A REGULAR RHYTHM. Of 10 cases with regular pulse rate, 3 showed a definite slowing, though in all the circumstances were such as to make them exceptional cases. One,

a case of advanced decompensation, showed for a few minutes only a drop in rate of 14; in one the rate fell to half of what it had been a few moments before, but this was speedily followed by a rise in rate and a fatal termination; and another, with paroxysmal tachycardia of auricular origin, resumed its normal rate. Seven were unaffected (Fig. 4).

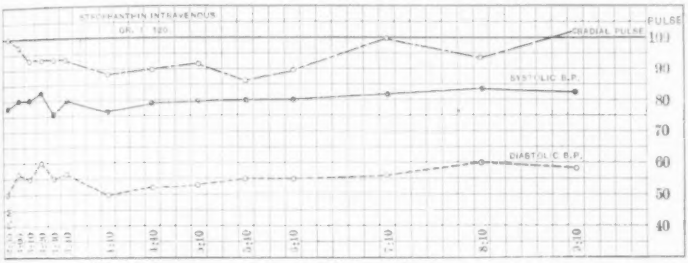

FIG. 4.—Case I. R. B. (regular rhythms). Showing action of $\frac{1}{120}$ gr. strophanthin. Effect very slight and transitory.

The cases reacting, all of them atypical, were as follows:

1. *Paroxysmal Tachycardia of Auricular Origin.* When first seen the attack had been going on for twelve days. Apex rate, 208 per minute and regular. Skin and mucous membranes moderately cyanotic, veins of the neck distended and fluttering rapidly. Heart one and one-half inch to the right and four inches to left of midline in the third interspace, with faint tic-tac sounds and no murmurs. Liver a trifle below the costal border; slight pitting of the skin over the tibiæ. Twelve days after the onset of this attack gr. $\frac{1}{60}$ strophanthin was injected, with no effect on the pulse rate. Eleven days later, the twenty-third day of the attack, gr. $\frac{1}{60}$ strophanthin was again administered at 9.30 P.M. One hour later there was no change, but when next seen at 8 A.M. the following morning the pulse was found to be 84, and remained at this rate thereafter. The patient volunteered the information that at midnight, following the injection, he had felt a sudden relief. Here again it is difficult to say whether the sudden relief was due to strophanthin or whether it was given coincidently with the spontaneous cessation of the paroxysm.

2. A patient, aged sixteen years, female, with mitral insufficiency and advanced decompensation, pulse rate 104 and regular, was given gr. $\frac{1}{60}$ strophanthin. In two hours the pulse rate had dropped to 84, but remained so only for a little while, and rose again steadily until her death, which occurred on the same day.

3. *Overdosage.* The patient, a colored girl, aged fourteen years, suffering with acute articular rheumatism, endocarditis, and pericarditis; pulse rate 124, regular rhythm. Weight eighty pounds;

$\frac{1}{60}$ gr. strophanthin was administered at 11 A.M. At 11.15 the pulse was 64 and of an irregular rhythm not determined, as there was no time to apply a polygraph. Immediately after, Cheyne Stokes breathing ensued, the pulse rate rose again to 110, and at 11.30 death occurred. In this case the dose was too great in proportion to her body weight and her serious condition. Though death seemed impending, there is no doubt that the strophanthin injection materially hastened it.

CONCLUSIONS. 1. The action of strophanthin administered intravenously is similar to that of other members of the digitalis group administered orally, but far more rapid.

2. Strophanthin had, in this series, a decisive effect in all cases with pulsus irregularis perpetuus. Where the pulse rhythm was regular, it showed an effect in only three instances out of ten, and this was both slight and transitory, except for the case of paroxysmal tachycardia.

3. In desperate cases of the pulsus irregularis perpetuus type, strophanthin administered intravenously will tide the patient over until digitalis, orally administered, has time to take effect.

4. In cases of the pulsus irregularis perpetuus type, the first effects are noted in twenty to thirty minutes, though the maximum may not be apparent for seven or eight hours. This effect lasts from three to ten days.

5. It does not seem advisable to give on any one occasion more than gr. $\frac{1}{60}$, and this, if repeated, should not be done before forty-eight hours; $\frac{1}{120}$ gr. has given a maximum result. On the other hand it may sometimes take more than $\frac{1}{60}$ gr. to produce this.

6. Two cases of paroxysmal tachycardia are reported with strophanthin administration, both followed by cessation of the attacks. It is not clear, however, to what extent the strophanthin was responsible for this phenomenon.

REPORT OF CASES WITH IRREGULAR RHYTHM.

CASE I.—Mitral stenosis; auricular fibrillation. Mrs. T. G. (service of Dr. James D. Heard, St. Francis Hospital), white, aged thirty-seven years. Complained of shortness of breath and cough. A previous history of chorea and acute rheumatic fever. On admission she had a diffuse precordial heave—a rough vibrating thrill—and a soft presystolic murmur rising in crescendo to a booming first sound. Pulmonic second sound greatly accelerated. Pulse was regular in rhythm and 120 to the minute. Lower border of the liver two and one-half inches below the costal margin. No edema. After two doses of ℳxv each of tincture of digitalis, she suddenly developed auricular fibrillation, which continued until her death five months later. After a few weeks she was discharged, with a pulse rate of 90 and feeling comfortable.

Two months later she returned to the hospital in an alarming state of decompensation—extensive swelling of the legs and abdomen, extreme orthopnea, a cough with frothy blood-tinged expectoration, and an irregular pulse of 160 to the minute, small and thready. The lower border of the liver extended 3 inches below the costal margin. There was marked congestion of the pulmonary bases and the heart sounds too tumultuous to analyze.

At 11 A.M. on the day after her second admission she received $\frac{1}{120}$ gr. strophanthin. Apex rate at this time was 160 per minute. At 11.30 her apex rate had dropped to 104 per minute and she was feeling comfortable. At 3.30 P.M. she received another dose of gr. $\frac{1}{120}$, bringing her apex rate in thirty minutes more to 100 per minute. At this time digitalis was administered by mouth and her lowered heart rate continued, aided by this oral administration. She left the hospital one month later in comfortable condition and with a heart rate of 84. The edema of her extremities and her engorged liver did not at once recede, but diminished slowly during the ensuing month.

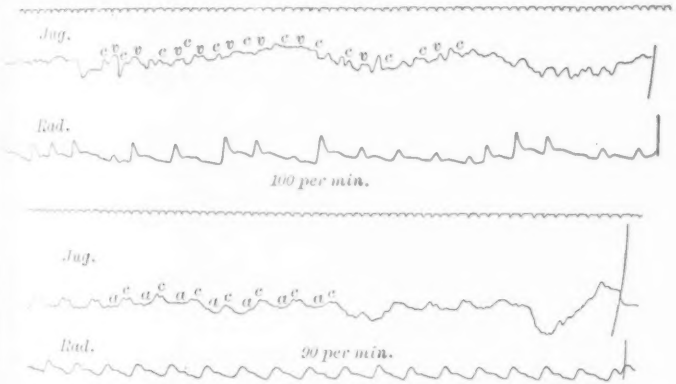

FIG. 5.—Case II (normal rhythm). Mr. S. Showing spontaneous reversion from auricular fibrillation to normal rhythm before operation.

CASE II.—S., male, white, aged sixty years; gall-stones; myocarditis; auricular fibrillation occurring in paroxysms. Patient was admitted for cholecystotomy. Pulsus irregularis; heart rate of 100. After three days in the hospital his heart suddenly reverted to a normal rhythm, with a pulse rate of 90. There was nothing in his treatment to explain this, save an unusually effectual enema.

Operation ensued and was successfully completed without any unfavorable results. Twenty-four hours after, he became dyspneic and cyanotic, and he again showed auricular fibrillation, with a heart rate of 144. $\frac{1}{120}$ gr. strophanthin was at once administered intravenously. Within an hour the pulse rate had dropped to

80 and, moreover, had resumed a regular rhythm. It remained so until the next day, when auricular fibrillation again was inaugurated, with extreme distress. A similar dose was again injected and a drop not only to the normal rate, but rhythm as well ensued within an hour and remained so until his discharge from the hospital in good condition one month later (Fig. 5).

Case III.—G. F., white, male, aged fifty-four years. Mitral insufficiency; myocarditis, auricular fibrillation.

The patient, an attorney, when seen had had an irregular heart action with dyspnea on exertion for four years, but had been incapacitated for only the past four months. The apex rate was 168, with slight pulmonary congestion, but no signs of congestion in other organs.

Strophanthin gr. $\frac{1}{120}$ given intravenously resulted in a drop to 120 within one and one-half hours. No further strophanthin was given, and the heart remained at this rate for three days, when digitalis orally administered on the first day in doses f3j per day began to take effect, and one week from the time that he was first seen the heart rate was 78 and the general condition so improved that he wanted to return to work.

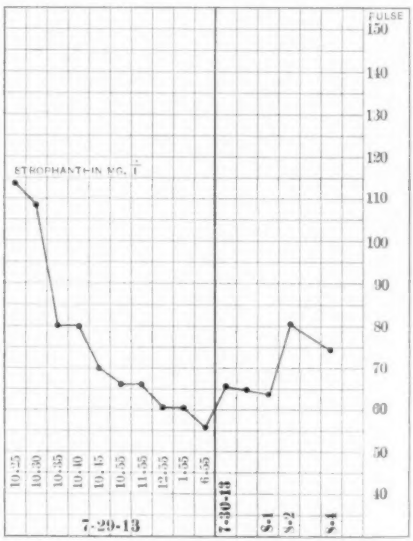

Fig. 6.—Auricular fibrillation. Case IV. Showing pronounced and rapid effect of injection of $\frac{1}{60}$ gr. strophanthin. The curve represents the apex rate.

Case IV.—S. L., female, white, aged twenty years. Mitral insufficiency and auricular fibrillation.

She never had rheumatism or chorea, but had suffered with a number of attacks of sore throat. Three years ago she began to complain of shortness of breath on the slightest exertion, which has continued with slight remission ever since.

On admission her heart rate was 120 per minute, and totally irregular. There were no signs of secondary congestion, and she was only moderately dyspneic. At 10.25 A.M. she received $\frac{1}{60}$ gr. strophanthin intravenously. At 12.30 her heart rate had dropped to 60. A few hours later it had further dropped to 55 and did not begin to go up again until the third day afterward. Her condition remained comfortable throughout (Fig. 6).

CASE V.—C. G., Italian, male, aged fifty years. Myocarditis, with auricular fibrillation. During the previous three years he had had a number of attacks of multiple arthritic pains, but had never been laid up. In the past year there have been occasional attacks of shortness of breath. No further symptoms. Venereal history negative.

On admission, pulsus irregularis; heart rate 140. Heart outlines two and a half inches to the right and four inches to the left of the midline in the third interspace. Cardiac respiratory murmur present, but no actual heart murmurs. Moderate cyanosis. Very slight pitting over tibiæ. Three injections of strophanthin were given (Fig. 3). March 13, $\frac{1}{80}$ gr. reduced the heart rate in three hours from 140 to 80, almost wiping out the pulse deficit. On March 17, the pulse having again risen to 100, $\frac{1}{120}$ gr. was administered with a drop to 75 in fifty minutes. On March 19, the pulse having risen again to 100, he was given a third injection of $\frac{1}{100}$ gr. with a drop in three hours to 68. He left the hospital one month later in excellent condition.

CASE VI.—J. D. (service of Dr. Nelson H. Clark, St. Margaret's Hospital), white, aged forty-four years. Myocarditis with auricular fibrillation. No history of rheumatic fever, chorea, tonsillitis, or any acute infection. Eight months ago, while at work, he became suddenly short of breath, and slight exertion since that time has brought on dyspnea.

RECORD OF TREATMENT.

	Apex.	Radial.	Systolic blood-pressure.
December 15, 9.45 P.M.	134	84	120
10.05 P.M.		Strophanthin, gr. $\frac{1}{102}$	
10.12	128	72	123
10.17 P.M.	132	54	130
10.22 P.M.	124	56	130
10.27 P.M.	118	56	135
10.35 P.M.	120	52	132
10.45 P.M.	115	48	130

		Apex.	Radial.	Systolic blood-pressure.
December 16,	4.25 P.M.	126	52	121
	4.32 P.M.		Strophanthin, gr. $\frac{1}{120}$	
	4.38 P.M.	110	76	130
	4.43 P.M.	90	84	125
	4.50 P.M.	96	88	125
	5.00 P.M.	94	84	125
December 22,	2.36 P.M.	104	..	118
	2.41 P.M.		Strophanthin, gr. $\frac{1}{120}$	
	2.46 P.M.	100	..	128
	2.51 P.M.	88	..	130
	2.56 P.M.	88	..	134
	3.01 P.M.	88	..	134
	3.06 P.M.	80	..	134
	3.11 P.M.	76	..	137
	3.16 P.M.	80	..	134
	3.21 P.M.	82	..	134
	3.26 P.M.	84	..	134
	3.31 P.M.	80	..	138

CASE VII. — Miss R. (service of Dr. Nelson H. Clark, St. Margaret's Hospital), white, aged thirty-eight years. Mitral stenosis—auricular fibrillation—with a previous history of rheumatic fever. The patient was a small, frail woman, very wretched on account of the nervous discomfort produced by the sensation of fluttering about her heart. More frequent injections were used with her than with any other patent. They occasioned her such prompt relief that she used to ask for them.

		Apex.	Radial.	Systolic blood-pressure.
November 3,	4.30 P.M.	108		
	4.35 P.M.	118		
	4.45 P.M.	112		
	4.50 P.M.		Strophanthin, gr. $\frac{1}{60}$	
	5.00 P.M.	90		
	5.05 P.M.	88		
	5.13 P.M.	84		
	5.18 P.M.	78		
	5.25 P.M.	76		
	5.30 P.M.	76		
	8.00 P.M.	74		
	9.00 P.M.	82		
	10.00 P.M.	70		
	11.00 P.M.	80		
	12.00 P.M.	80		
November 20,	9.35 A.M.	132	96	65
	9.40 A.M.		Strophanthin, gr. $\frac{1}{70}$	
	9.45 A.M.	128	88	78
	9.50 A.M.	100	84	95
	9.55 A.M.	88	83	95
	10.00 A.M.	86	84	
	11.00 A.M.	88	85	
	1.00 P.M.	..	78	
	2.00 P.M.	..	78	
	3.00 P.M.	..	68	

Eight more similar injections were given, with like result, and the patient to the present time prefers this form of treatment to oral administration.

Case VIII.—J. B., white, male, aged forty years. Coal miner. Auricular fibrillation, with myocarditis. No history of previous infections. Several months previous to admission he experienced shortness of breath, with a fluttering sensation, while at work. He is quite comfortable when at rest. Apex rate 110; $\frac{1}{60}$ strophanthin caused a drop in one hour to 84, the effect lasting for two days.

Case IX.—M. B., white, aged thirty-six years. Lobar pneumonia, with grave toxemia. Auricular fibrillation, with a heart rate of 160. No dilatation. Two days before his death he received $\frac{1}{60}$ gr. strophanthin, with a drop in heart rate in one hour to 80. The patient's condition remained unimproved, and the heart rate again rose steadily to 150. On the following day he received another injection, with a similar drop, but in spite of this, he became progressively worse, and died the same evening.

Case X.—A. S., Italian, aged thirty-six years. Lobar pneumonia, with severe toxemia and delirum. Auricular fibrillation, dating back three years. Heart rate, 144. Twenty-four hours before his death, which occured on his third day in the hospital, he received gr. $\frac{1}{60}$ strophanthin. One hour later the apex beat was 92. His general condition, however, remained unaffected, and with the heart rate rising again steadily, he died the same day.

CASES WITH NORMAL RHYTHM.

Case I.—R. B., white, female, aged sixteen years. Mitral insufficiency and stenosis. Pulse regular, 100 per minute. Gr. $\frac{1}{120}$ strophanthin caused a drop of eight beats in her pulse rate. It quickly rose again, and by evening the rate was again 100 (Fig. 4).

Case II.—E. O., female, aged fourteen years. Mitral insufficiency and stenosis, with early decompensation, acute pericarditis, a frail girl; heart, one and one-quarter inches to the right of midline and three and one-half inches to the left in the third interspace. Pulse 120, regular; occasional edema of the ankles; mitral systolic murmur, pericardial frictions. Liver two fingers' breadth below the costal border. Strophanthin $\frac{1}{60}$ gr. produced no effect on the pulse rate. Later she was given tincture of digitalis by mouth, 1 dram a day, until she took 10 drams in all, when it was discontinued, owing to slight headache. The pulse at this time showed occasional slowing, due to a heart-block which had been induced, but which disappeared two days after discontinuing the digitalis.

Case III.—H. M., aged sixty years. Aortic insufficiency. Pulse 130, regular. Strophanthin $\frac{1}{100}$ gr. reduced the pulse rate from 130 to 125, but within an hour it had risen to the original rate;

it seems scarcely reasonable to interpret so slight a difference as the result of the injection.

CASE IV.—Mrs. C., aged forty-two years. Mitral insufficiency; beginning of decompensation; regular pulse rhythm, 120 per minute. Strophanthin $\frac{1}{60}$ gr. had no effect upon her pulse rate.

CASE V.—C. R., male, aged forty-two years. Mitral insufficiency; pulse rate 110, regular; $\frac{1}{60}$ gr. strophanthin had no effect on his pulse rate.

CASE VI.—Mrs. B., aged thirty-five years. Seen after laparotomy; temperature 22, pulse 120, regular but weak and thready. Strophanthin $\frac{1}{80}$ gr. injected to note any possible effect; the patient was in a serious condition at the time it was given. The injection not only had no effect, but the pulse continued to rise steadily to 180, maintaining its regular rhythm throughout until the time of her death, which occurred the second day.

CASE VII.—B. H., male, aged forty years. Arteriosclerosis; myocarditis; pulse rate, 100. No evidences of decompensation. Dose used $\frac{1}{60}$ gr. There was no lowering of the pulse observed.

CASE VIII.—F. B., male, aged forty-one years. Paroxysmal tachycardia of auricular origin. Myocardial insufficiency. Pulse rate estimated by polygraph, 208 per minute; when seen, the attack had lasted twelve days, coming on without apparent cause in the middle of the night. No history of any previous infections. Skin and mucous membranes moderately cyanotic. Heart apex in the fifth interspace three and a quarter inches from the midline. No murmurs present; liver border, one finger breadth below the costal margin. Strophanthin $\frac{1}{60}$ gr. injected without effect. Edema of the legs came on; the apex of the heart extended out from the midline and the liver gradually went down to the level of the umbilicus. Eleven days after the first injection a second injection of $\frac{1}{60}$ gr. was given at 9.30 P.M. Two hours later no change had been noticed; when next seen, on the following morning, the pulse rate was 84 to the minute and regular. It remained so for the rest of his stay in the hospital. While it is not known at what time the drop in pulse rate began, the patient stated that at midnight following his injection he experienced a sudden relief, and the change in rate probably occurred suddenly at this time.

CASE IX.—A. M., female, aged twenty years. Mitral insufficiency, with advanced decompensation. Had not improved to any extent under oral administrations of digitalis, although she had received in all eight drachms of the tincture. With the onset of nausea, digitalis was discontinued. She continued unimproved and gradually weaker and more dyspneic. Two weeks following the discontinuance of digitalis, and at a time when she appeared to be growing extremely weak, she was given an injection, $\frac{1}{60}$ gr. strophanthin. The pulse rate at the time of giving the stophanthin was 104, and an examination made an hour subsequently showed

that the pulse rate had dropped to 86, but within eight hours it had risen again and death occurred on the same day. Although no records were made with the polygraph, there is little doubt that most of the apparent slowing in this instance was due to the production of extrasystoles.

CASE X.—C. W., colored, aged fourteen years. Endocarditis; pericarditis; acute articular rheumatism. Patient when seen was sitting up in bed, gasping and very weak: pulse rate was regular, and 124 to the minute. It was decided to give her an injection of $\frac{1}{60}$ gr. strophanthin, with the fatal effect observed in the previous discussion.

THE VALUE OF COLONIC INFLATION IN THE DIAGNOSIS OF CHRONIC APPENDICITIS.[1]

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THE frequent association of chronic inflammation of the appendix with persistent gastro-intestinal disturbances is being more and more recognized, but the diagnosis of chronic or subacute appendicitis is, nevertheless, a matter of no little difficulty, particularly in those cases which have had no history of a previous acute attack. In many instances, pain in the right iliac fossa, either spontaneous or induced by pressure, furnishes the clue to the diagnosis, but in many other instances there is an absence of this feature, the chief symptom being abdominal pain of more or less definiteness. Granting that there is well-marked pain in the right iliac fossa, one is still not justified in concluding that the cause of the pain is appendicular in origin, without excluding disease of organs situated in the right upper and lower quadrant of the abdomen, notably the Fallopian tube, ovary, kidney, and gall-bladder, a matter at times beset with difficulty.

The frequent occurrence of latent appendicitis and the difficulty attending its diagnosis has led Bastedo to advance a new test, the dilatation test, in order to determine the presence of chronic appendicitis. He passes a colon tube, eleven or twelve inches, into the rectum and injects air by means of an atomizer bulb. "If, as the colon distends, pain and tenderness to finger-point

[1] Read at a meeting of the American Gastro-enterological Society, Atlantic City, June 22 and 23, 1914.

pressure become apparent at McBurney's point there is appendicitis," to use Bastedo's own words.[2]

The test is not needed in an acute appendicitis and is not required in an undoubted chronic case, but the indication for the method lies in individuals with persistent digestive and abdominal disturbance for which no cause can be found. Also in distinguishing between right-sided pelvic inflammation and an inflamed appendix the test is said to be of assistance. Bastedo concludes his article with the statement: "In the use of the test during the last four years we have had no case in which the test was positive and the operation findings negative. But in two out of all our cases the negative finding of the test was followed within six months by a typical attack of appendicitis, and the test was, therefore, presumably at fault. Several times in the early days of the test surgeons operated for a suspected appendicitis, though the test was negative, and in every such case the appendix was found normal."

Such promise of an easy method of diagnosis has led subsequent observers to study the test, among them being Dreyer,[3] Rost,[4] Slawinski,[5] and most recently Hertz.[6] The last-named is particularly enthusiastic and agrees with Bastedo, to wit, that the test is an almost infallible means of diagnosing chronic appendicitis. He warns against its use in cases of acute inflammatory disease of the appendix unless the surgeon is prepared to operate at once, as there is imminent danger of tearing adhesions or causing a diseased appendix to perforate.

Hertz has shown that the only stimulus to visceral pain is distention, but so long as the colon is healthy the pain appears no sooner in the appendix than in the rest of the colon. If there is inflammation of the appendix there is an increased response to the pain stimulus of visceral distention, pain is much more rapidly produced, and as a result, local pain and tenderness are observed in the right iliac fossa. Adhesions do not seem to be the main factor in the production of the pain, as some cases exhibited typical pain without these being present.

Rost[7] claims that the test is not a specific one for appendicitis, but that the condition of the lower bowel may be similarly recognized by the pain which follows colonic inflation. He quotes, as exemplifying this contention, a case of cecum mobile, which after a fixation of the cecum experienced no pain on inflation, and a case of pain in the left iliac fossa which was shown at operation to be due to chronic adhesions.

Slawinski[8] has made use of the method for some time and suggests that it be called Bastedo's test.

[2] Amer. Jour. Med. Sci., 1911, cxlii, 11.
[3] Münch. med. Woch., 1912, p. 1845.
[4] Ibid., 1912, p. 2055.
[5] Ibid., 1912, p. 2055.
[6] Lancet, 1913, i, 816.
[7] Loc. cit.
[8] Loc. cit.

The preciseness of the results claimed for colonic inflation has induced us to study the patients admitted to the Presbyterian Hospital during the past year.

The technique employed was as follows: The patient being in a recumbent position, a rectal tube, well greased, is introduced into the rectum for a distance of about three inches. (It is unnecessary to insert the tube as far as eleven or twelve inches as recommended by Bastedo). After the tube has been introduced the patient lies on his back, an atomizer bulb is attached to the free end of the tube, which is brought up between the legs and air is slowly pumped in. In individuals with no appendicular disease there is no pain apart from a feeling of fulness in the lower bowel, with at times a sensation as if defecation was imperative.

In patients suffering from appendicitis it is claimed that there is an almost immediate complaint of spontaneous pain in the right iliac fossa, much exaggerated by finger-point pressure. In those cases of appendicitis with epigastric pain, pain is not complained of in the epigastrium, but in the right iliac fossa, and in cases with pain located in this region the discomfort is intensified. At times pain on pressure over the distended cecum induces pain, not over McBurney's point, but also in the epigastrium as well; this phenomenon being only seen, however, when epigastric pain has been a preëxisting symptom. Aaron[9] has already described as a sign of chronic appendicitis epigastric pain which follows pressure in the right iliac fossa.

While pursuing our studies it was deemed advisable to examine every patient admitted to the medical ward, provided he complained of no abdominal distress. By doing this we collected about seventy-five cases, presumably normal, so far as the appendix was concerned, and in none was pain complained of in the right iliac fossa following inflation. We feel that this number of cases justifies the belief supported by the experience of Bastedo and of Hertz that normal individuals do not have what may be called positive tests. We therefore discontinued our observations on control cases.

In studying the abdominal cases admitted to the hospital, our work was much facilitated by the ready willingness of the various chiefs of the Presbyterian Hospital, who at all times gladly placed their material at our disposal. We cannot express too strongly our appreciation of the many courtesies extended by Drs. Hodge, Rodman, Jopson, Shoemaker, and Girvin, in whose wards many of the operative cases were observed.

Our results briefly put are not in accordance with those of other writers. There have been in our series of positive tests 3 cases which have had no indication of appendicular lesion; notably 1

[9] Jour. Amer. Med. Assoc., 1913, lx, 350.

case of cholelithiasis, 1 of nephritis (signs present one day, absent the next; patient later died of uremia), and 1 of right-sided pneumonia, with pain in the right iliac fossa.

Of the negative cases, 7 had appendices chronically inflamed and bound down by adhesions and 5 were suffering with acute appendicitis.

Salpingitis, in our experience, does not give typical pain in the right side. It is true that pain is complained of, but it is low down in the abdomen and not in the region of McBurney's point. We have felt that the sign may have some value in distinguishing between this condition and appendicitis.

Conclusions. 1. Inflation of the colon is an equivocal means of diagnosing chronic appendicitis. Some cases have negative tests and some have positive; there seems to be no constancy in the result obtained.

2. In acute appendicitis the method should not be employed. It is rarely necessary as a diagnostic aid, as the results are uncertain and the risk of injurying the intestine is too great.

3. The method should not be considered useless, however, for at times the diagnosis has been materially strengthened by its employment, and operation has later shown the wisdom of our faith in the result obtained. Inflation of the colon, however, should be regarded merely as an aid in the diagnosis, history and physical examination being far more valuable.

4. We have seen no positive reactions in normal individuals.

5. The test is in no sense pathognomonic of chronic appendicitis.

DUODENAL ALIMENTATIONS.[1]

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Perhaps the best of the many excellent things which Einhorn has contributed to the science and practice of medicine is the duodenal tube and its practical application to the relief of certain disorders of the alimentary tract. Duodenal alimentation has been practised during the past four years by an increasing number of medical men throughout the United States, Canada, and Europe, and wherever it has been intelligently carried out it has gained a permanent place in the treatment of suitable cases. Whenever duodenal alimentation has failed it has been due, in my opinion,

[1] Read by invitation before the Pittsburgh College of Physicians, February 26, 1914.

to one of two causes, which have ever in the past operated to bring into temporary discredit many excellent methods of instrumentation, namely, inappropriate application or faulty technique.

The demands which duodenal alimentation satisfy and which give it the right to a permanent place in medical means and measures are the almost complete rest of the stomach, with lessened activity of the duodenum, and the supplying of sufficient calories for maintaining the individual's nitrogen balance and body weight. No other method, except feeding into the stomach itself, is capable of sustaining life for more than short periods of time. I have often fed patients continuously and exclusively for four weeks by this method, and in one instance the patient was so fed for five weeks without during this period, once removing the tube, and with a gain of five pounds in weight. This patient had had recurrent symptoms of duodenal ulcer during several years previously, and had been treated with more or less temporary benefit in several of the large cities of Europe before coming to America. She had had, now and then, quite pronounced hemorrhages from the bowel, accompanied by some symptoms of collapse. Her other symptoms were also more or less typical. After the removal of the duodenal tube she quite rapidly resumed her normal diet and accustomed round of duties, and has remained in good health during the two years which have elapsed since the termination of the treatment.

This case is only one from a large number of similar cases, and is cited to answer two oft-repeated questions, to wit: whether this method is suitable in duodenal ulcer cases, and whether there is danger in leaving the tube *in situ* over long periods of time.

The principal field of usefulness for duodenal feeding is in the treatment of gastric and duodenal ulcers, but it may be and is used with equal benefit in pylorospasm from any cause, provided the bucket can be gotten through the pylorus. The relief from pain afforded some of these patients is almost as marked as that afforded by hypodermic medication.

There is another class of very trying cases in which this method of feeding acts most happily—namely, gastroptosis and gastrectasis with or without ischochymia, in which, owing to the low position of the stomach or to atony of its musculature, the stomach is incapable of propelling the food on into the duodenum with sufficient rapidity to supply the body needs. These patients rarely fail to respond promptly to duodenal feeding if properly carried out.

I am treating duodenal catarrh by inserting the duodenal tube, and after washing the mucosa with water I allow 500 c.c. of a 1 to 500 solution of argyrol to flow in more or less rapidly so as to distend the gut. Two or three such treatments repeated at intervals of three or four days rarely fail to relieve these patients.

In several cases of inoperable cancer of either the cardia or the pylorus, accompanied by increased pain during and after meals,

I have been able to pass the tube into the bowel and institute duodenal feeding, with marked relief, for some time. In such cases we must be careful not to leave the tube *in situ* until the stenosis reaches a degree where it becomes impossible to withdraw it on account of the size of the gold bulb.

Another class of cases in which duodenal feeding may often prove of benefit is the severe vomiting of pregnancy. This method should at least be tried before resorting to more extreme measures. The only difference in applying this treatment in these cases is that the duodenal tube should be somewhat longer and so be introduced far down in the jejunum. I have tried this in only one case, and it proved successful to the extent that we were able to tide the patient along until the fetus was viable, thus enabling the mother to give birth to a living child.

Einhorn is using duodenal feeding in cirrhosis of the liver and has noted some striking results therefrom, a report of which he gave in an excellent paper which he read before the sixteenth annual meeting of the American Gastro-enterological Association. I quote the summary with which Einhorn closed his paper: "During duodenal alimentation in all the six patients the liver became markedly smaller (already after two or three days), assuming a size almost normal. In four patients the result was lasting. In one, however, a few days after the termination of feeding the liver began to grow larger, while in another patient with pure cirrhosis and dilated heart the size of the liver quickly assumed its original large proportions. The influence of duodenal feeding was in this case very marked but not lasting.

"My experience thus far justifies me in the conclusion that duodenal alimentation contributes greatly toward diminution of the functional work of the liver. This rest treatment for the latter organ is of benefit, whenever it is considerably impaired. The cirrhosis of the liver and allied conditions accompanied principally by swelling of the hepatic tissues form a field in which duodenal alimentation may be applied apparently to a great advantage."

In idiopathic hyperchlorhydria, which resists all other measures, duodenal feeding usually affords relief by reducing the hypersensitiveness of the gastric mucosa. In these cases the treatment should be prolonged for three or four weeks to secure permanent results.

Another important use I have made of the duodenal tube is in the treatment of amebic dysentery. For a long time ipecacuanha has been recgnized as the most powerful medicament in the treatment of amebic dysentery. It has, however, always been difficult to administer this drug in sufficient amounts to effect a cure on account of its emetic action. By introducing the tube well down into the gut and forcing an emulsion of ipecacuanha through it a sufficient dosage may be administered to check the action of the

ameba coli in the gut, and thus in some cases cure the disease. It is often necessary to repeat the dose several times at intervals covering a period of several weeks to finally control the disease. Rarely, if ever, has vomiting been induced by the ipecacuanha when given through the duodenal tube. It is necessary to prepare the patient for this treatment by giving a sharp purge the day before and limiting the food to liquids. After administering the ipecacuanha it is wise to have the patient remain in bed for the ensuing twenty-four hours. After considerable experience with this method, and with emetin given hypodermically, I feel that perhaps the duodenal tube method is as reliable as the hypodermic method, and the duration of treatment is likely to be shorter. Another point in favor of the duodenal tube is that the patient can readily be taught to give it to himself should the case prove stubborn, necessitating several repititions of the procedure.

In the light of maturer experience in the treatment of amebic dysentery by emetin which Dr. Vedder, of the United States Army, has had, the results of which are set forth in his splendid article,[2] the following conclusions may be drawn: Emetin has the power to kill the vegetable ameba in the tissues, but has no effect on the entameba hystolytica, since they still persist in the stools of individuals who have had a thorough course of treatment with emetin; whereas the ipecacuanha given through the duodenal tube destroys the entameba hystolytica in the intestinal tract, but has very little effect on the ameba in the tissues. Therefore, it would seem that the best results might be secured by the use of the combined methods, to wit: giving the emetin hypodermically in small daily doses and giving the ipecacuanha through the duodenal tube once or twice a week for several doses.

As I have already mentioned the fundamental indication calling for the use of the duodenal tube is rest for the stomach and duodenum. Therefore all those bodily conditions which are benefited by putting this part of the alimentary tract in splints call for this method of treatment. The second indication for the use of the duodenal tube is for the administration of foods or medicine in such amounts as would otherwise be rejected by the stomach. The third indication is to secure duodenal contents for examination to aid in diagnosing certain disorders of the digestive system beyond the stomach.

As to the limits of usefulness of duodenal alimentations, it may briefly be said that they will be determined by the dictates of the rules which apply to other methods used in such cases.

Contra-indications to the use of duodenal tube are few: for instance those cases where the degree of stenosis is such that the bulb does not readily pass the obstruction, and in those rare cases

[2] Jour. Amer. Med. Assoc., February 14, 1914.

where there is such hypersensitiveness of the mucosa of the throat as to induce constant retching and pain. Now and then we find an individual whose duodenal mucosa is so hypersensitive that each feeding causes purging regardless of the kind of food administered. Happily these cases are rarely met.

In those cases where the pylorospasm, from whatever cause, has persisted so long as to impair the patient's general health to a degree demanding immediate relief of the stenosis, we should advise operative interference.

In this connection I wish to say that moderate hemorrhage from the esophagus, the stomach, or the duodenum is no contra-indication to the employment of the duodenal tube.

Einhorn's apparatus consists of a small gold bucket perforated by several small openings, and capable of being taken apart for the purpose of cleaning: a rubber tube of small caliber leading to the bucket; a rubber pet-cock and a feeding table, an ingenious arrangement which rests over the glass of nourishment so that the food may be drawn up through one tube into a glass syringe, and by manipulation of the pet-cocks be forced slowly into the tube connecting with the duodenal tube, without disconnecting the syringe.

The technique is as follows: At night the patient with the aid of water swallows the duodenal tube. During the night the bucket will usually pass into the duodenum. I have found it is well to give one-half grain of codein one hour before the tube is introduced, to allay the spasm of the throat and to insure a quiet night's rest. The second line on the tube is supposed to be at the incisor teeth, the bucket is at the pylorus, and when the third mark has reached the teeth the end of the tube is probably *in situ*, well down in the duodenum. When this is accomplished the tube is allowed to remain in place during the entire course of treatment. During the first twenty-four hours some of the patients have been somewhat uncomfortable from sore throat, due to the presence of the tube in the throat; but this has never been severe enough to occasion the withdrawal of the tube on this account, and usually in from twenty-four to forty-eight hours they have become accustomed to it and do not mind it.

How can we tell that the tube is through the pylorus? By slight traction a resistance is felt if the tube is in the duodenum; aspirations through the tube with a glass syringe bring typical, golden-yellow, duodenal juice of neutral or feebly alkaline reaction and not acid gastric juice; lastly, if the patient is given a glassful of milk and water to drink, and if aspiration is immediately performed, the milky solution will not be returned through the tube if the end is in the duodenum, as it would were it still in the stomach.

The feedings are given at two-hour intervals during the day. The food which has been most satisfactory is a mixture of milk,

raw eggs, and sugar of milk. Not infrequently individuals are met in whom eggs are not tolerated; in these patients eggs produce distress after the feeding, and if persisted in give symptoms of acute ptomain poisoning. The amount of food which should be given at a feeding is from 150 c.c. to 300 c.c. of milk, one raw egg, and 15 gm. of sugar of milk. It is wise, however, to begin with smaller quantities, 100 c.c., and work up to the full amount as soon as possible.

It is important that the feedings simulate nature's method as nearly as possible, and to this end the food must be heated and strained and then given slowly through the tube. Under ordinary circumstances the stomach performs, among its other duties, the function of withholding food from the duodenum until of a correct temperature. Too hot foods are cooled and cold foods are not propelled from the stomach until they are warmed to the body temperature. It is important to bear this in mind in undertaking duodenal feeding, as the duodenum is most sensitive to variations in temperature, reacting to each shock, as well as to too rapid administration of food, by causing a feeling of nausea, discomfort, restlessness, clammy perspiration, etc. After each feeding the duodenal tube must be carefully cleaned by forcing a syringeful of water through it, followed by a syringeful of air, after which the pet-cock is closed before the syringe is disconnected. Failure to keep the tube clean will result in its becoming entirely blocked by a trough coagulum of milk and egg, which will necessitate frequent and annoying withdrawal of the tube.

As previously reported, the first two cases which I treated by the duodenal method of feeding were unable to take a sufficient quantity of nourishment at a feeding without producing untoward symptoms of nausea and distress, and therefore I modified the method in the following manner: Instead of the syringe I make use of the gravity and drop method, as in giving salt solution by the Murphy method. The duodenal tube is connected to a tube leading from a pint irrigating jar, and the flow regulated so that the 300 c.c. used at a feeding takes about twenty-five minutes to pass through. The milk may be kept warm by having the conducting tube pass through hot water or under a hot-water bag, etc.

During the period of duodenal feeding, in order to increase the amount of fluids supplied to the body, normal salt solution may be given every day by the drop method through the rectum.

Case I.—Aaron S., aged forty-nine years; night watchman. Family history negative. No history of venereal disease. Healthy up to six years ago, when the symptoms for which he later came to me made their appearance. At that time a diagnosis of biliary colic was made by another physician and the gall-bladder was opened and drained. No gall-stones or other disease was found. Later on, the symptoms still persisting, appendectomy was done,

with no relief. He first came to me in the early part of January, complaining of burning pain in the stomach, coming on three or four hours after meals, and which was relieved by the taking of food or alkalies. He had also acid regurgitation. The physical examination was negative except for a spot of tenderness on pressure over the lower right-hand quadrant of the epigastrium. The thread test was positive for gastric ulcer, showing a blood-stain 50 cm. from the incisors. The *x*-ray report was as follows: "There is a deformity of the duodenal cap which is probably spasmodic in origin. A six-hour residue, which is due to pylorspasm. These findings are confirmatory of ulcer of the stomach."

FIG. 1.—Case I. Mr. A. S.

On January 15 the patient was put upon duodenal feeding, which was maintained continuously for eighteen days. At the end of the first twenty-four hours all the gastric symptoms had disappeared; a few days after the withdrawal of the tube he was able to resume a practically normal diet, excluding only the more irritating articles of food. At the present time he is entirely free from symptoms.

CASE II.—Herbert H., aged twenty-five years; single; private secretary. Family history negative. No venereal history. Had an attack of jaundice six years ago lasting one month. When he came under my observation he had been suffering for two months from an acute severe pain beneath the inner half of the right costal border, which extended through to the right scapula, coming on about two hours after lunch. The chest organs were normal, so also were the liver and kidneys. There was a tender point on

pressure beneath the inner half of the right costal arch. The thread test was positive for duodenal ulcer, showing a stain 57 cm. from the incisors. The *x*-ray report was as follows:

"The absence of a well-defined cap in three sets of radiograms and the rapid emptying of the stomach are confirmatory of duodenal ulcer." The patient was put on duodenal feeding for two weeks, at the end of which time all symptoms had disappeared. Two weeks after the withdrawal of the tube he was eating a liberal, though soft diet, and has remained well.

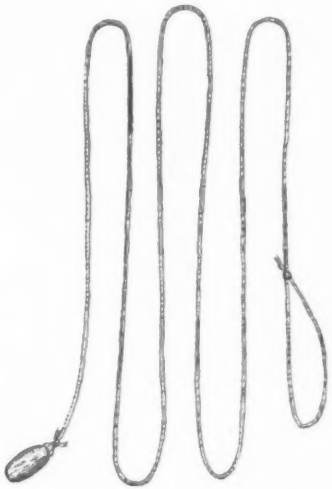

FIG. 2.—Case II. Mr. H. R. P.

CASE III.—Timothy T. A., aged forty-one years; married; Congressman. Family and venereal history negative. Had been healthy up to nine years ago. During the past seven years had had increasing digestive disorders. In August, 1912, had severe hemorrhage from the bowels, at which time a diagnosis of duodenal ulcer was made, for which he was operated upon. The diagnosis was confirmed at the operation. The ulcer was not excised, but a purse-string suture was used and the ulcer turned in.

He came to me the following January with a history of having passed blood from the bowel almost daily since the operation. He was pale, almost chalky. The conjunctivæ and lips were bloodless. The hemoglobin was 33 per cent.; red-blood cells, 3,000,000; leukocytes, 5200. The chest organs were normal, so also were the liver and kidneys. Examination of the feces showed them to contain a large percentage of coagulated blood. The thread test was positive for duodenal ulcer, showing a blood

stain 68 cm. from the incisor teeth. No *x*-ray examination was made in this case, as the diagnosis was so obvious and immediate treatment urgent. He was put at once upon duodenal alimentation, and within five days the macroscopic blood had disappeared from the stool, and within three weeks the feces were negative for occult blood, and have remained negative since that time. The tube was left *in situ* for twenty-eight days. On withdrawing it his diet was gradually increased to solid but bland foods, on which he remained until the latter part of the summer, since which time he has been eating his normal diet. The condition of the blood gradually improved until it is practically normal, the hemoglobin being now 81 per cent.

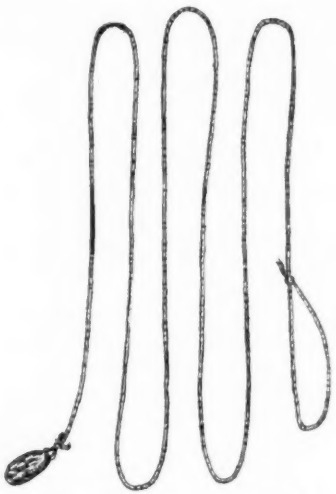

FIG. 3.—Case III. Mr. T. T. A.

In a former paper I called attention to an interesting case of tic douloureux, which appeared to be almost entirely cured by a course of duodenal alimentation. In this case the patient had already previously determined that there was a distinct connection between her attacks and the condition of her stomach. She could often foretell the appearance of an attack. This case proved to be one of extreme gastroptosis with gastrectasis, and with a marked degree of hyperacidity of the gastric juice. Duodenal alimentation was carried out for four weeks and brought about an almost complete cure. During the years which have elapsed since that treatment the patient has suffered only momentary "jabs" of pain in the affected area, and these occurred only after some dietetic indiscretion. It is interesting in this connection to note that the lower

border of her stomach has gradually come up from the upper border of the symphisis pubis to practically the normal position. This result may be expected in a large majority of cases of gastrectasis, provided a suitable line of treatment is carried out in addition to the duodenal feeding.

The cases cited above are merely to illustrate what may be accomplished with duodenal alimentation.

TUBERCULOSIS OF THE BRONCHIAL GLANDS AND LUNG HILUS: A CLINICAL AND RADIOGRAPHIC STUDY.[1]

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Frequency of the Condition. By whatsoever route tubercle bacilli enter the body, be it through the alveolar wall, the bronchial mucous membrane, or by way of the gastro-intestinal tract, they ultimately reach the bronchial glands in the great majority of instances.

In a series of 569 cases of tuberculosis, Comby[2] found the bronchial glands involved in all, and Hamburger and Sluka observed a like condition in 110 cases. Haushalter and Fruhinsholz[3] found the bronchial glands tuberculous in 74 out of 78 infants dying of acute tuberculosis, or tuberculous meningitis.

As commonly used, the term bronchial glands includes the glands at the sides of the trachea and the group just below its bifurcation, as well as the glands surrounding the bronchi.

The largest ones are usually found below the right bronchus. The tracheal group are in relation to the superior vena cava and the vagus and recurrent laryngeal nerves. Owing to the lower origin of the left recurrent nerve, it is in contact with the trachea for a longer distance than the right one, and more often shows the effect of pressure by paralysis of the left vocal cord. When the glands attain a large size, they may press upon the arch of the aorta and its branches, the innominate veins, and the phrenic nerves.

The pericardium is anterior to the infratracheal group, and the

[1] Read before the Hartford Medical Society, June 15, 1914.

[2] Quoted by Grenet, Anal. d. Méd. et Chirg. Infant. Paris, 1911, xv, 497.

[3] Archiv. d. Méd. d. Enfant, 1902; quoted by Grenet, op. cit.

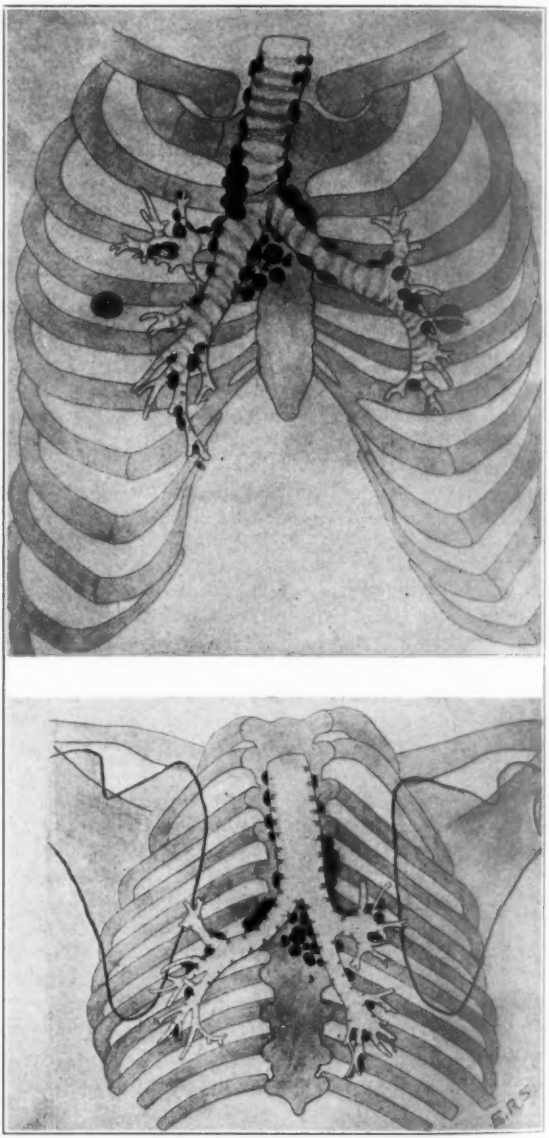

FIG. 1.—Composite drawings showing the relationship of the bronchial glands to the thoracic wall in the adult. The glands are according to Sukiennikow (Berl. klin. Woch., 1903, xi, 316, 347, 369) and the trachea and bronchi are after Blake (AMER. JOUR. MED. SCI., 1899, cxvii, 320). In the child the trachea bifurcates at about the level of the intervertebral disk between the fourth and fifth thoracic vertebræ, which corresponds nearly to the tip of the fourth thoracic spine. This is about opposite the articulation of the third costal cartilage anteriorly.

esophagus is behind and slightly to the left. The vagus nerve is also in relation to this group. The hilus glands are in contact with the lung and the bronchial and pulmonary vessels. The location of the several groups is shown in Fig. 1.

Leroux[4] has stated that the glandular lesion is usually unilateral from the second to the fifth year, but that after that period it is more apt to be bilateral. Harbitz[5] found the oldest lesion more often in either the hilus, infratracheal and peritracheal groups than in the bronchial glands proper. Up to the fifteenth year the glandular form of tuberculosis predominates, but after that age the pulmonary form is more common.

Just how the infection of the lung is brought about we do not know, though much experimental work has been done. The belief has been quite general that the bacilli after penetrating the alveolar wall or bronchial mucous membrane are promptly borne by the lymphatics to the bronchial glands. Here they may remain until the lymphatics, becoming obstructed and dilated, reverse their flow and the tuberculous lymph backs up into the lung. As early as 1876 Parrot[6] opposed this theory. He stated that he was always able to find a lesion in the lung that was older than the glandular one, though a diligent search might be required to discover it, as it was not infrequently very small. So constant were his results that he taught his pupils that the bronchial glands were "the mirrors of the lungs."

Others have since confirmed his results, and Ghon[7] has reported finding a primary lung lesion in 92 per cent. of 184 cases. The lesion was frequently small and often single. Ghon considers the latter fact good evidence against the theory of infection from a reversal of the lymph current. Inasmuch as it is commonly taught to search the apices for the earliest sign of tuberculous disease it is especially noteworthy that the primary focus was more often found in the lower lobe than in the upper.

Shika[8] has recently stated that in six years of *x*-ray work, devoted wholly to children, he found only three cases of apical tuberculosis.

Harbitz,[9] studying the modes of dissemination of tuberculosis in children, found that the lungs were commonly infected through the rupture of a caseous gland into a bronchus, usually near the hilus. This resulted in a caseous bronchopneumonia in the distribution of this bronchus.

By the use of the *x*-rays, Sluka[10] found that the hilus of the lung,

[4] Archiv. d. Méd. d. Enfant, 1908; quoted by Grenet, op. cit.
[5] Jour. Infect. Dis., 1905, ii, 143.
[6] Mémories d. l. Soc. de Biol., 1876, p. 308.
[7] Der primäre Lungenherd bei der Tuberkulose der Kinder, Berlin, 1912 (Ed. Jour. Amer. Med. Assoc., 1912, lix, 1544).
[8] Wien klin. Woch., 1914, xxvii, 173. Abs. AMER. JOUR. MED. SCI., 1914, cxlvii, 770.
[9] Loc. cit.
[10] Wien. klin. Woch., 1910, xxiii, 156.

as well as the glands, was always involved in young infants, and frequently in older children as well.

SYMPTOMS. We do not know how long after infection takes place before symptoms and physical signs develop. Straub[11] is of the opinion that the primary lung focus is not accompanied by symptoms, and that they do not appear until the bronchial glands and adjacent lung becomes involved. Usually the onset is insidious, and the symptoms, which are those of a toxemia, are suggestive rather than conclusive, but their vagueness should awaken our suspicion. They often start from childhood, frequently developing after whooping cough or measles. A sense of weariness is usually present, and if the patient be a child, inquiry will show that he does not romp and play with the other children, but listlessly "sits around." The appetite is usually capricious, and the child is often irritable. Sometimes complaint is made of a sharp pain within the chest, which may radiate to the shoulder. Again, an interscapular backache may be almost constant. Vague digestive disturbances may predominate the scene, suggesting a mild form of muscular insufficiency. Phillippi[12] found hyperchlorhydria rather common. Persistence of these symptoms in a young adult who is below weight calls for investigation of the lung hilus region, as the apical signs may be equivocal or absent. The temperature is often subnormal, especially in the morning, though an afternoon rise is usually present. Occasionally the cheek on the side of the lesion will flush with every little excitement; rarely are the pupils unequal.

Often, perhaps usually, the patient has a cough; when brassy and "explosive" in quality it is extremely suggestive of bronchial adenopathy. These children "catch cold" easily, and with each cold the already swollen lymph nodes become somewhat larger, and pressing on the vagus a cough develops. The cough not infrequently causes gagging, and sometimes even vomiting occurs. But it should be much more generally appreciated that cough may be insignificant, and even entirely absent, as it was in the child whose radiograph is here shown (Fig. 7). Night sweats seem to be the exception, rather than the rule.

It has been found that infants with tuberculosis of the bronchial glands are prone to attacks of dyspnea, in which the stridor is chiefly or wholly expiratory in character, thus differing from thymic asthma, in which the dyspnea is inspiratory. As the disease progresses, the dyspnea affects both inspiration and expiration. In a number of instances the condition has been mistaken for one of laryngeal diphtheria, and intubation has been performed, but without relief. The persistence of the voice in bronchial aden-

[11] Beit. z. Klinik. d. Tuberk., 1912, xxiv, 283.
[12] Ibid., 1911, xxi, 67.

opathy and its absence in diphtheria should make this mistake infrequent.

In Guisez's case,[13] where the dyspnea was mechanical from glandular pressure, passage of the bronchoscope brought instant relief.

Very alarming symptoms may arise from the rupture of a caseous gland into the trachea or a bronchus. The child in apparently good health is suddenly seized with extreme dyspnea and death may occur before assistance can be obtained. Goodman[14] has recently collected from the literature a number of such cases. Some years ago Hall[15] reported the recovery of a patient after coughing up a caseous gland which had ruptured into his bronchus. Perforation of the esophagus has also occurred, and death has immediately followed the erosion of one of the large bloodvessels (Fisher,[16] Barry[17]).

There is nothing more puzzling to the physician than the patient who spits blood, but has no sign of a pulmonary lesion. It is probable that in some cases the blood comes from the rupture of a vessel in the mucous membrane of a bronchus overlying a tubercle, possibly the primary focus. In other cases, coughing causes a rupture of a bloodvessel already distended from the pressure of enlarged bronchial glands (Griffin,[18] Barthez and Rilliet[19]).

A few years ago we had as a patient a boy who had a number of profuse hemorrhages. Repeated examination disclosed only signs of bronchial adenopathy—increased whisper interscapularly (D'Espine sign). We have recently been informed that he has developed well-marked signs of pulmonary involvement.

Physical Signs. *Inspection.* While peribronchial tuberculosis can often be recognized in the adult, it is more common in children, and the signs are usually more marked in early life. The child is usually, but not always, frail. Some years ago, one of us (Stoll) found, by means of the von Pirquet tuberculin test, that the delicate child was about four times as apt to be tuberculous as his more robust playmate.

Dilated veins interweaving across the chest usually indicate glandular pressure, though in one case where they were particularly marked, both physical signs and the *x*-rays were negative. Expansion may be diminished at one apex, which will be seen to "lag" with inspiration. If the breath be held at the end of inspiration and one observes the hilus region (anteriorly comprising that part of the upper two interspaces between the midclavicular and parasternal lines), an apparent retraction will frequently be noted

[13] Bull. Soc. d. Pediat. de Paris, 1911, No. 3, p. 114.
[14] Jour. Amer. Med. Assoc., 1913, lxi, 1442.
[15] Amer. Jour. Med. Sci., 1899, cxvii, 185.
[16] Lancet, London, 1909, i, 28.
[17] Med. News, 1885, xlvii, 236.
[18] Med. Rec., New York, 1891, xxxix, 166.
[19] Quoted by Coley, A Practical Treatise on the Diseases of Children, 1846, p. 185.

on one or both sides (Figs. 2, 3, 4, and 5). Usually this is only a simulated retraction, and is occasioned by the failure of this particular part of the chest to expand. This "dimpling" of the hilus region with inspiration is best seen when the patient is seated in a slanting light from a side window. The patient should be turned from side to side, as an oblique light brings out the depression best. The maximum depression is usually in the second interspace. In patients with hilus disease of long standing, when cicatrization has taken place, a well-marked depression is constantly present. Only rarely have we found the sternomastoid muscle of the affected side in spasm. In a few instances the intercostal

FIG. 2

FIG. 2.—R. P., aged fourteen years. Bilateral hilus disease of several years' duration. Aortic second accentuated and "cog-wheel" breathing, with harsh inspiration over left hilus. Posteriorly slight paravertebral dulness and d'Espine's to the fifth thoracic spine.

FIG. 3

FIG. 3.—R. H., aged fourteen years. Bilateral "hilus dimple" and whispered voice over the sternum to the fourth cartilage. Bilateral paravertebral dulness and very marked d'Espine's to eighth thoracic spine. The *x*-ray picture shows a "well-marked shadow to the right of the vertebral column above the cardiac shadow (paratracheal glands).

muscles over the hilus region showed some rigidity, but we have not been able to feel the confidence in this sign that Pottinger[20] does. Noeggrath[21] was able to demonstrate Head's zones—areas of superficial tenderness— in the majority of the children examined who were suspected of having tuberculosis. The areas involved were those supplied by the second, third, and fourth thoracic and the fourth cervical, which suggests disease of the base of the lungs and the bronchial glands.

[20] Jour. Amer. Med. Assoc., 1909, lii, 771; also AMER. JOUR. MED. SCI., 1909, cxxxvii, 669.

[21] Jahrb. f. Kinder., 1911, xxiv, 74; reviewed by Michael, Amer. Jour. Dis. Child., 1912, iii, 180.

Firm pressure over the sternoclavicular articulation and over the midthoracic vertebral spines may elicit pain. This is only present when the disease is active.

FIG. 4

FIG. 4.—H. B., aged fourteen years. Dilated veins, slight dulness, and bilateral "hilus dimple." Rales . . . Posteriorly, whispered bronchophony heard throughout the interscapular space. For the *X*-ray findings see Fig. 8.

FIG. 5

FIG. 5.—L. H., aged fifteen years. Bilateral "hilus dimple" and slight retraction below right clavicle. Inspiration cog-wheel and in the first two spaces on the left very harsh. The intercostal muscles overlying were in slight spasm, as was the sternomastoid of that side. Aortic second was accentuated and the whispered voice was present over the whole of the sternum and throughout the interscapular space. For *x*-ray see Fig. 10. Her history as given by her mother is quite typical. "Never robust; always 'ailing;' subject to colds with cough; often sore throats; strength and appetite poor. Is irritable and indisposed to play. Recently pain across the chest."

Percussion. Percussion, if sufficiently delicate, is a valuable diagnostic measure, but as usually performed so much normal lung is set into vibration that the dull note from the diseased focus is completely lost. In a former paper[22] this is discussed at length. Both a light and very light stroke should be employed, the latter being only a tapping with the middle finger of the right

[1]Amer. Jour. Dis. Child., 1912, iv, 333.

hand upon one of the terminal phalanges of the left hand, which is held firmly against the chest. It is as important that the finger be held firmly against the chest wall as it is that the blow should be a light one. Ewart[23] has happily referred to this very light percussion as "the percussion of the deaf," which means that the "feel" is as significant, perhaps, as the note obtained.

Dulness from the bronchial glands is sometimes met with anteriorly in the upper two interspaces in the parasternal line, more often on the right side. One should be familiar, however, with the slight degree of dulness normally present in the first interspace to the right of the sternum. A dull note over the sternum is rarely due to enlarged bronchial glands, but may be caused by enlargement of the glands of the anterior mediastinum. In children it is usually caused by an enlarged thymus, and, as a rule, extends to the left in the first interspace for a centimeter or more.

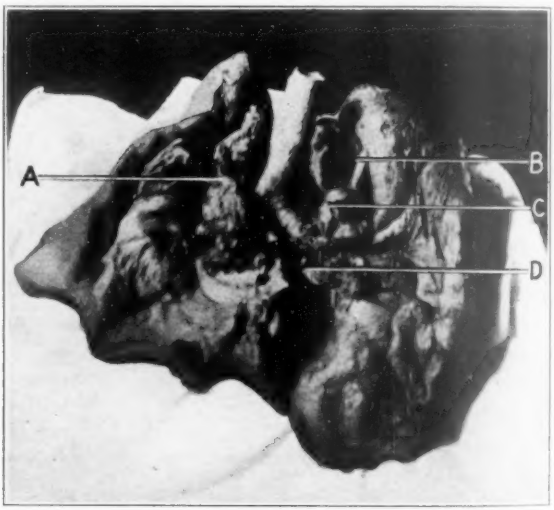

FIG. 6.—Enlarged bronchial glands in the case of H., who had had a marked d'Espine's sign for several years. An anterior view, the heart having been removed. *A*, large group of glands to the right of the trachea and above the right bronchus; *B*, cross-section of aortic arch; enlarged glands; *C*, above left bronchus; *D*, under left bronchus. The infratracheal group not enlarged.

Percussion posteriorly is usually more valuable than anteriorly. Ewart, long a champion of percussion of the spinous processes, has recently become an advocate of paravertebral percussion, which Kramer,[24] Nagel,[25] and others consider much superior to percussion of the spinous process.

[23] Prog. Med., 1913, xv, 68.
[24] Beit. z. klin. d. Tuberk., 1909, xv, 337.
[25] Jahrb. f. Kinderheil., 1908, 68, 46.

The relation of the hilus to the posterior chest wall is shown in Fig. 1. It is somewhat higher in children than in adults. Bing[26] has described a normal hilus dulness of limited extent, which is more pronounced on the right. More recently, Ewart[27] has drawn attention to the fact that the area of normal hilus dulness changes with respiration, being wider with expiration and narrowing at the end of the full inspiration. A "suppression of the inspiratory oscillation" on one side he considers indicative of a pathological process of that side.

As the outer border of dulness is usually the most difficult to determine, it seems to be of more practical value to observe the differences in the note at the sides of the vertebræ at the extremes of the respiratory act rather than to depend upon the differences in size of the dull area, though this is sometimes evident. As a rule, we have not been able to feel sure of the "normal hilus dulness" in healthy children, when percussing during quiet respiration.

It does not seem that very slight dulness in this region is sufficient evidence of enlarged bronchial glands, unless accompanied by other signs. Nor does the absence of dulness exclude glandular enlargement. For posterior percussion, a patient should be seated on a stool, with arms well crossed over the chest. The head is slightly inclined forward, and the upper and inner border of the lungs is outlined by König's method. The normal curve of the inner border reaches the vertebral column between the second and third thoracic vertebræ. With enlarged tracheal glands this border is often displaced outward. A dermatographic pencil is used, and one should verify his findings with closed eyes. Dulness is most commonly met with at the sides of the fourth and fifth thoracic vertebra, and more often on the right than on the left. It seems probable that the glands are not alone concerned in this dulness. The engorgement of the bloodvessels and lymphatics, which exists in the hilus region during the acute stage, is in all probability an important factor. The unsuccessful attempt to locate a golf ball in a loaf of bread by percussion strengthens this opinion. The increase of dulness noted at the end of expiration is in part due to the diminution in the air content of the lung and also to the increased congestion which Sewall and Childs[28] have shown attends that period of respiration. Direct percussion of the vertebral spines has not proved as satisfactory as paravertebral percussion. With a large mediastinal tumor a dull note may be obtained over the fifth and sixth thoracic spines.

Auscultation. Grancher[29] maintained that a diminution of the respiratory murmur was an early sign of enlarged mediastinal glands. We have met with this but twice. Once in a woman with

[26] Ugesk. f. Laeger, 1910, lxxii, 199.
[27] Loc. cit.
[28] Archiv. Int. Med., 1912, x, 45.
[29] Bull. gener. de Méd., 1906, lxx, No. 36; abstract Jour. Amer. Med. Assoc., 1906, xlvii, 2041

advanced Hodgkin's disease, and the other time in the child whose *x*-ray is here shown (Fig. 7).

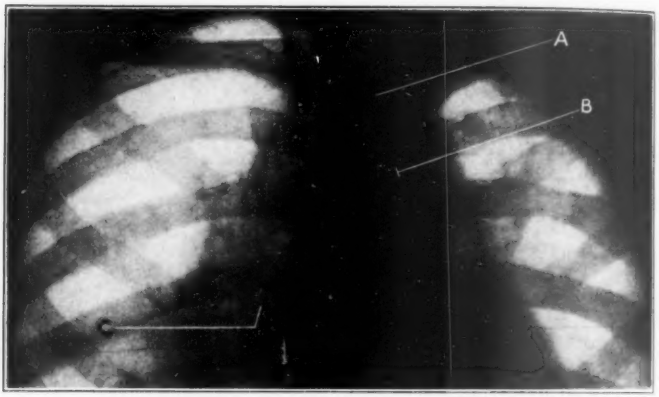

FIG. 7.—H. A., aged ten years. Referred by Dr. W. G. Murphy. There was slight dulness in the two right interspaces near the sternum. Very dull in the third space, extending to the parasternal line. Respiratory sounds much diminished over right lower lobe. A few rales in inner third first interspace and over lower lobe. Posteriorly no paravertebral dulness but d'Espine's sign, more marked on the left than on the right, was heard as low as the inferior angle of the scapula. Aortic second sound accentuated. The *x*-rays show extensive disease of the right hilus. The inner end of line *C* indicates the right border of the heart. The left border of the trachea is indicated by *A*. Line *B* shows the beginning of the left bronchus. Notwithstanding this extensive lesion this child had no cough. A footnote refers to the autospy findings in this case.

A harsh inspiration, often "cog-wheel" in type, was sometimes heard over the hilus region anteriorly. The *x*-rays showed hilus disease of the side where this type of breathing was noted in several cases, and we are inclined to think this may be a valuable sign of hilus involvement. In one instance the *x*-rays showed bilateral hilus disease, and the harsh inspiration was noted only on one side. In this case there was spasm of the intercostal muscle over the area of harsh inspiration, suggesting that this was the more active lesion. In one patient the breathing was quite bronchial near the spine of the left scapula.

In a considerable number of children with signs of enlarged bronchial glands, one may detect fine crepitations in the vicinity of the nipple. They may be apparent only on coughing, and are not to be confused with atelectatic rales, which disappear after one or two deep breaths. Miller and Woodruff[30] found that the children with these rales gave a much higher percentage of positive reaction to tuberculin than other children.

[30] Jour. Amer. Med. Assoc., 1909, lii, 1016.

Several times an accentuation of the aortic second sound has been noted, and in one such case coming to autopsy there was a group of enlarged glands between the aorta and the chest wall.

Of particular importance is the character and distribution of the voice and especially the whispered voice. In the normal individual if the stethoscope be pressed firmly against the chest wall, the area of transmission of the whispered voice is slight. Anteriorly it is normally heard throughout the first right interspace, and in the inner half of the left, and posteriorly it is not present below the seventh cervical spine in children and the fourth thoracic in adults.

There is a peculiar quality to the whispered voice that is of the greatest significance. It consists in a continuation of the sound for a moment after phonation has ceased. It is best brought out by having the patient whisper "three thirty-three" (children can usually say "tree, tree, tree" more easily), when it will be observed that the final "e" of the last word "three" has an echoing quality and persists a moment after speech has ceased. This postphonal element alone is significant. For many years, D'Espine[31] has diagnosed enlargement of the bronchial glands by this sign alone. He observed that in children the tracheal quality of the whispered voice did not normally extend below the seventh cervical spine. When heard over the upper thoracic vertebræ, he considered it indicative of bronchial adenopathy. It is usually heard for a variable distance at one or both sides of the vertebræ, and to be of significance in adults it should extend at least as low as the fifth thoracic. The diagnostic import increases with the area of distribution.

Sewall[32] attributes the whispered bronchophony to congestion of the lung parenchyma, and he considers it the earliest evidence of tuberculous infiltration. In a few of our cases, where stereoradiographs were taken, the fine lines were seen to extend to the surface of the lung in the interscapular region, which would seem to support Sewall's theory. From the result of the autopsy findings in four of our cases, however, we are inclined to think that the glands lying along the trachea and bronchi play a large part in the transmission of the tracheal quality to the whispered voice.

The intensity of the bronchophony, moreover, is usually much increased by flexing the head well forward, which carries the trachea and bronchi with their glands backward toward the vertebral column.

This sign was well marked in three out of four adults in the Hartford Hospital, with aneurysm of the aortic arch, presumably from pressure on the left bronchus. Both Zabel[33] and Koch[34] have

[31] Bull. Acad. de Méd., 1907, lvii, 167.
[32] Loc. cit.
[33] Münch. med. Woch., 1912, lix, No. 49; Jour. Amer. Med. Assoc., Abs. 1913, lx, 250.
[34] Tribune Med., 1912, viii, 381; quoted by Da Costa, Amer. Jour. Med. Sci., 1913, cxlvi, 660.

observed it in cancer of the esophagus, though whether from metastasis in the bronchial glands or direct pressure on the bronchus was not known.

Increased whisper is much less common anteriorly, though it is occasionally heard over a considerable part of the sternum or along its border. It is sometimes present in the anterior axillary line just under the lower border of the pectoralis major muscle.

Several children in whom D'Espine's sign was present a few years ago, have improved much in health since coming under observation, and both the intensity of the whisper and its area of distribution are notably less.

Not only should one observe the quality of the voice, but auscultation should be performed when the patient coughs, for occasionally one will observe an echoing quality to the cough, even in the absence of whispered bronchophony.

D'Espine has had several autopsy confirmations of the value of whispered bronchophony in diagnosing enlarged bronchial glands. In a previous paper (Stoll[35]), drawing attention to the value of whispered bronchophony in the diagnosis of tuberculosis in the aged, mention was made of finding enlarged glands in two adults who had had this sign. A third case has since come to autopsy. The complete history has been given elsewhere. The important points are as follows: Mrs. A. H., aged sixty-four years, had hemorrhage and cough "off and on" for many years, and with each attack she would "run down." The most noteworthy sign was the large area between the scapulæ over which D'Espine's sign was present. She died last winter, after a few days' illness, of a double pneumonia. The bronchial glands, especially the tracheal group, were much enlarged, as the accompanying photograph (Fig. 6) shows. No giant cells were found in either of two sections which Dr. J. C. Rowley kindly examined for me, though there was much pigmentation.

In only one case have we been able to compare the *x*-ray findings with a postmortem examination.[36] Louis G, aged two years, was admitted to the service of Dr. Charles Goodrich at the Hartford Hospital, May 28, 1912, because of enormously swollen cervical glands. Through Dr. Goodrich's courtesy the child was examined several times. There was dulness over the sternum and in the first three left interspaces as far out as the midclavicular line. Posteriorly well-defined dulness to below the spine of the scapula, extending $1\frac{1}{2}$ inches to the right of the spinal column and 1 inch to the left. The breath sounds were somewhat diminished and slightly tubular in quality. At the first examination the cry was

[35] Boston Med. and Surg. Jour., 1912, clxvii, 291.

[36] Since this article was written another case has come to autopsy. The *x*-ray being Fig. 7. There was advanced disease throughout right lung with large tuberculous bronchial glands. This will be reported later with photographs.

thought to be indicative of enlarged glands, but a note was made a few days later that there were "no auscultatory signs of enlargement of the bronchial glands." Yet, nevertheless, we felt that the glands were enlarged. Two months later, during which time the child had steadily failed, the dulnesses mentioned before had diminished very much, and a few scattered rales and small areas of bronchovesicular breathing had developed. The cervical glands diminished markedly in size during the last weeks of illness.

The *x*-rays showed the fine markings were very much increased, and extended to the periphery of the lung. Along the course of these interweaving thread-like lines were small dot-like shadows, giving the appearance of knots tied in thread. The largest of these were about the size of a pinhead. There was considerable increase in the shadow above the heart at the right root, which was incorrectly attributed to bronchial glands. As the picture was taken while the child was crying very hard and holding its breath, the shadow was probably a distended superior vena cava. In a second *x*-ray, taken just after death, this shadow was very much less.

The autopsy revealed no enlargement of the bronchial glands. The mediastinum was somewhat congested, and a few small tubercles were scattered throughout the lungs. A small group, the largest being pinhead in size, was found just under the pleura of the left upper lobe, and was apparently shown in the *x*-ray. The mesenteric glands were much enlarged and several were broken down.

It seems probable that the dulness noted anteriorly when the child first came under observation was due to an enlarged thymus, which decreased in size during the long illness, until at death scarcely a trace remained. The diminution of the dulness toward the last of the illness favors this theory. That the *x*-rays do not show thymic enlargement may be due to its being taken with the child on its back.

The impairment of resonance to the right of the upper thoracic vertebræ may have been the result of congestion of the hilus vessels.

It is conceivable that enlarged bronchial glands might have diminished in size coincidently with the cervical group, but not that they should show no enlargement at autopsy.

The infection of the lungs was evidently hematogenous from a mesenteric or cervical gland, and death occurred before the bronchial glands were involved.

The venous hum heard over the upper part of the sternum when the head is retracted does not seem to be a sign of value.

As to the value of tuberculin, we are still of the opinion, expressed elsewhere,[37] that "Even when the tuberculin test is positive, we have to fall back on the symptoms to ascertain whether we are

[37] Loc. cit.

dealing with clinical tuberculosis which needs immediate treatment, or with only an anatomical lesion which requires temperance in all things."

RADIOGRAPHY. The large central shadow observed in the normal thorax is due to the heart and mediastinal contents. Extending out laterally are the heavy shadows caused by the large or stem bronchi. On the right side both ascending and descending bronchi are distinctly seen, but on the left, due to the intervention of the cardiac shadow, the greater part of the descending bronchus is not visible. The density of these shadows increases with age, being, as a rule, much heavier in the adult. Radiating from these coarser markings are finer lines which project into the lung field for varying distances, but do not extend normally to the surface of the lung. These markings are produced by the walls of the bronchi and the blood and lymph vessels with their contents.

Dunham and Boardman[38] found that in early tuberculosis these fine lines often reach the periphery of the lung at the site of the lesion. While our series of stereoscopic plates is small, in a number of instances we have observed this. In the infant with early miliary tuberculosis above referred to, which came to autopsy, the most distinctive feature was the filling of both lung fields with fine interweaving lines. In other cases where these lines did not extend into the lung field for any considerable distance, they were much more numerous and heavier than normal about the hilus region. In a few instances we have seen near the root small "soft" shadows with hazy irregular borders which are well shown in the stereoscopic negatives from which Fig. 8 is made. Fine lines can be seen connecting these shadows with the lung root. This is apparently an early involvement of the lung parenchyma in the hilus region. In non-stereoscopic negatives we have observed a shadow which is in the position normally occupied by the superior vena cava. This shadow is concave to the right, while the one caused by glands is convex, and is, moreover, of greater density, and protrudes farther into the lung field. It extends from the tip of the third cartilage upward toward the clavicle, giving an increased width to the root of the lung. Since drawing attention to this shadow in 1910[39] a number of other observers have mentioned it as an early evidence of enlarged bronchial glands. Involvement of the parenchyma in the hilus region is usually roughly wedge-shaped with the apex at the hilus. When the disease is but slightly active the shadow borders are usually sharp. In the more acute cases the shadow is softer and the border often ill-defined (acute exudative type of Cole). Because of the interposition of the cardiac shadow the infratracheal glands are usually not seen.

[38] Bull. Johns Hopkins Hosp., 1911, xxii, 229.

[39] Proc. National Association for Study and Prevention of Tuberculosis, 1910, vi, 252; also AMER. JOUR. MED. SCI., 1911, cxli, 83.

It is impossible for one who has not studied stereoscopic negatives to appreciate their superiority over the single plate method. While a lesion may be distinctly shown by the later process its exact situation cannot be determined. It is desirable for the

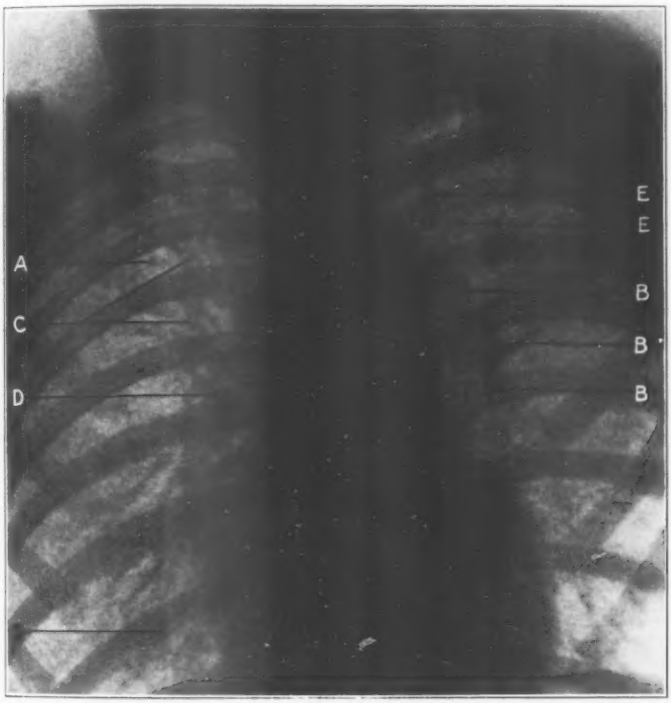

FIG. 8.—Stereoscopic appearance. (For physical signs see legend with Fig. 4.) Anterior view. The distortion of the mediastinal contents is due to the rotation of the chin to the right. In the upper lobe the fine lines approach almost to the lung surface, and in the first interspace there are two small tubercles just below the surface: *A*, at the left root are a number of tubercles which are arranged in three different layers resembling mountain ranges (*B*, *B*, *B*). In the lower part of the left upper lobe are observed several small shadows (*E*)of little density and with an ill-defined and irregular border. These are connected by fine lines with the root and are presumably early tuberculous foci. Posteriorly the finer markings extend to the surface of the right lung in the fifth (*C*), eighth, ninth, and tenth interspaces. A number of tubercles are seen at the root (*D*) and throughout the lower lobe.

clinician to learn to interpret his own radiographs, as only by this means can he satisfactorily compare his physical signs with the *x*-ray findings. All our cases were examined and the physical signs recorded before being radiographed.

TECHNIQUE. The method we find most desirable, and the one giving us the best soft-tissue detail, is as follows: With the patient in the erect position a moderately soft tube is placed approximately six feet from the plate (14 x 17 mounted in a screen). A small diaphragm is used and an exposure of one-half to one second is made. For stereoscopic work we use an automatic plate-changing device. The right oblique position has not proved very satisfactory.

FIG. 9.—J. L., aged seven years. Eczema as infant, whooping cough when one and a half years old, and ever since has had a cough. When first examined in 1909 had small moist rales over upper two-thirds of both lungs. Well-marked d'Espine and a small area of bronchovesicular breathing at the inferior angle of left scapula. The rales have cleared up except a few at both bases, and the most marked whisper is heard just internal to inferior angle of left scapula. Stereoscopic appearance: The right descending bronchus is much heavier than normal. An increase of lines from right apex to root (*A*) is to be observed and a haziness of the whole of the apex. The fine lines extend to the surface of the lung in the third, fourth, fifth, and sixth (*B*) interspaces left and the first, second, third, and fourth interspaces of the right side when viewed from behind, but in the anterior view the line markings do not reach the surface. The fine lines at the lung root are increased. Several tubercles can be seen at *C*.

TREATMENT. When diagnosed early the usual out-of-doors treatment for tuberculosis will usually suffice. Children so affected should attend an open-air school, as there are few environments more disastrous to health than the usual overheated, unventilated school-room. In several instances we have given tuberculin therapeutically with seemingly good effect. One child in particular, whose cough at night was very distressing, experienced great

relief from tuberculin treatment. Interruption of the treatment was followed by a recurrence of the cough, which again became less upon the resumption of tuberculin. This sequence of events was repeated several times, as it was impossible to make the mother realize the necessity of keeping up the treatment. Dr. H. W. Brayton made a number of blood-counts before and after the

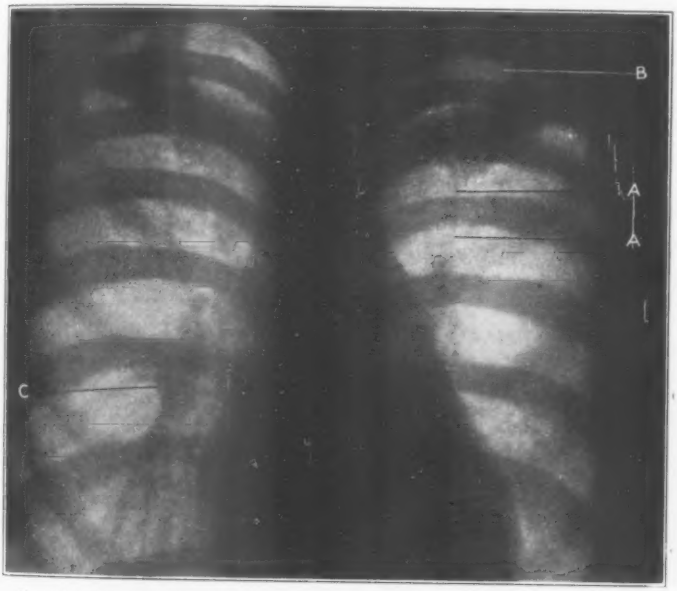

FIG. 10.—Stereoscopic appearance. L. H. (For physical signs see legend with Fig. 5.) Anterior view. The fine lines (*A*) extending upward from the left root to the apex are somewhat increased and slight cloudiness to the whole left apex (*B*) above the clavicle. At the right root, opposite the third rib, an enlarged bronchial gland (*C*) can be seen in which are a number of tubercles. The lines radiating from the right root, especially those standing downward, are heavier and more numerous than usual. None of the fine lines extend to the surface in the anterior view, but when examined from behind the fine lines extend to the periphery in the fifth interspace. The clinical diagnosis was "involvement of the bronchial glands and right root." The lesion at the left apex was not recognized, though it should have been because of the harsh inspiration and muscle spasm.

tuberculin injection, and did not observe that the lymphocytes were increased after the tuberculin injection, as Schulz[40] claimed they were.

When the lung adjacent to the glands is shown by means of the *x*-rays to be involved, Straub and Otten[41] advise making an artificial pneumothorax.

The gradually increasing dyspnea is difficult to deal with. Believing that he was operating for the relief of the dyspnea from

[40] Beitr. z. klin. d. Tuberk., 1911, xxi, 79. [41] Loc. cit.

an enlarged thymus, Veau[42] exposed a mass of caseous bronchial glands, which he removed. Betke[43] also operated successfully on a woman, aged twenty-nine years, who had tracheal stenosis from tuberculous glands at the bifurcation of the trachea.

It is possible that with the more general adoption of one of the methods by which the thoracic cavity can be explored with impunity, operative relief in these cases will become the rule.

Such excellent results have been obtained in thymic dyspnea by *x*-ray treatment, that it seems it should be thoroughly tested in enlarged bronchial glands.

Mention has been made of the relief of the dyspnea from the passage of the bronchoscope. This can only take place when the dyspnea is due to actual pressure of a gland on the trachea, and it is a procedure of much hazard, for if the instrument should perforate the already bulging and diseased tracheal wall the result would probably be disastrous. As the dyspnea in most cases is the result of a vagus neuritis rather than a mechanical pressure, it would seem that the usefulness of the bronchoscope in these cases is not great.

The urgent dyspnea from the rupture of a gland into a bronchus or trachea calls for immediate relief. If the patient is not able to expel the disintegrated gland by coughing, a tracheotomy should be performed and a large catheter, with the end cut off, so that the opening is at the end, passed downward. In the cases where the obstruction is due to pus, aspiration might be life-saving. In Goodman's case, insufflation caused the pus to be discharged through the tracheotomy wound by the sides of the tube.

Conclusions. 1. Prior to the fifteenth year, tuberculosis of the bronchial glands and lung hilus is the most common form of tuberculous disease.

2. The early symptoms are usually indefinite and chiefly of toxic origin. While a cough is generally present, it may be entirely absent even with advanced disease of the bronchial glands.

3. Although the orthodox signs of incipient (apical) tuberculosis are not present in these cases—in fact, the primary lesion is often in the lower lobe—there are certain physical signs which are indicative of a pathological process at the lung root.

4. The significant signs are a "hilus dimple" (noted anteriorly over the hilus region at the end of inspiration), dilated veins, parasternal and paravertebral dulness, and most significant of all, a well-marked whispered bronchophony in the interscapular region (d'Espine's sign).

5. Radiography, and especially stereoradiography, is of the utmost value in these cases, as it shows the exact location and extent of the morbid process, and is the greatest stimulus to careful clinical work.

[42] Bull. Soc. de pediat. de Paris, 1911, No. 2, p. 83.

[43] Berl. klin. Woch., 1913, No. 4, p. 197; quoted by Goodman, op. cit.

HEREDITARY ATAXIA.

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The hereditary ataxias form a large and important group of nervous diseases, the accurate subdivisions of which often cause uncertainty and confusion. The various types, such as the spinal ataxic paraplegia, Friedreich's spinal ataxia, and Marie's cerebellar ataxia may combine enough symptoms of each form to make the definite grouping most difficult.

The cases reported in this paper show this tendency and cannot be definitely placed in either group, though resembling most the cerebellar type of Marie. The spastic, springing, or bouncing gait with some degree of ataxia is most peculiar and the extent of the athetoid and choreiform movements with the decided ataxia of the muscles of the face, tongue, and throat, the extremely ataxic speech, and the late onset of the disease, are all out of the ordinary.

The spinal type of hereditary ataxia described by Friedreich develops usually before the age of puberty, in most cases about the age of ten years. The history is generally one of a steadily increasing clumsiness first noted in the child's running and jumping during his play. This gradually increases, and choreic and at times athetoid movements develop, most active in the arms, but often including the head, and causing a peculiar purposeless bobbing or nodding of the head. Nystagmus occurs, the speech becomes slow and drawling and later ataxic, and the patient's mentality deteriorates; this latter, however, is not so frequently true as in the cerebellar type.

Ordinarily sensory changes are not present, though later observers record some loss in position sense, compass point discrimination, etc. The bowel and bladder are unaffected. The patellar reflexes are often absent and Romberg's sign is positive. Scoliosis and deformities of the feet and legs, with the characteristic Friedreich's toe, may occur and are seldom found in the other forms. Tremor of the hands, tachycardia, excessive sweating, and fragilitas ossium are some of the less common symptoms and really not characteristic of the disease.

In the cerebellar type described by Marie, Fraser, and Nonne the symptoms often resemble very much those of Friedreich's disease, and the two may be combined clinically and pathologically, one or the other form preponderating. In Marie's cerebellar ataxia the symptoms are more those of cerebellar involvement, such as the staggering, drunken gait, explosive ataxic speech, ataxia of the

extremities, etc. The onset is later, usually after the age of puberty; spastic ataxia and paraplegia are absent or occur late in the disease, while the ataxic speech defect, mental deterioration, and jerky tremors are more apt to be prominent symptoms of the cerebellar form. Optic neuritis is not uncommon. The knee-jerks are preserved and, as a rule, active. There is no decided Romberg swaying in typical cases.

In the hereditary ataxias the spinal cord or the cerebellum, or both, as the case may be, show congenital underdevelopment. In addition the lateral and posterior columns of the cord are sclerosed in Friedreich's ataxia, while in the cerebellar type the principal findings are atrophy and sclerosis of the cerebellum. Pathological changes have also been reported in the cerebral cortex, the meninges, and in the cells of the spinal cord.

Where the lateral columns of the cord are more or earlier affected the case may be grouped under the spastic ataxic paraplegias; the speech defects, bone deformities, etc., are uncommon in these types. It is, however, only a subclass of the Freidreich group and would better be considered as such.

Cases of juvenile tabes and the neural type of progressive muscular atrophy and multiple sclerosis have some symptoms in common with the hereditary ataxias and might lead to some difficulty of diagnosis in the earlier course of the diseases. Like most hereditary diseases the hereditary ataxias are transmitted more often by the female members of the family. Direct inheritance from one generation to the next is not very common, but in most cases the intermediate family or generation show other forms of degeneracy, such as epilepsy, insanity, imbecility, etc. Nothing can be done for the direct betterment of these patients other than temporarily making them as comfortable as possible and relieving any unusual symptoms. The disease once developed steadily progresses, very occasionally, however, showing a long retardation of the symptoms. Any definite help to families so affected can only be along a eugenic line.

Case I.—J. D., aged fifty years, farm laborer up to six years ago; married. Eight children living and well so far as he knows; five boys and three girls. Three healthy brothers, aged thirty, thirty-seven, and forty years, and one similarly affected. Maternal grandfather had same disease; time of onset not known. His mother had the same trouble; date of onset not known. She died aged fifty-three years. Patient's first symptom started when he was aged forty-four years, as a general clumsiness.

During the examination the patient would require two or three minutes to answer a simple question, during this time making an intense effort to speak. He would move his arms, shoulders, and legs, elevate the eyebrows, move his mouth, roll his eyes, and finally answer in a slow, broken, drawling, ataxic manner.

His mouth and tongue movements were ataxic and the rolling of the tongue and twisting of the mouth could be seen during his efforts to shape them for a reply. Sometimes he would struggle so long that he would forget the question.

He says it is more difficult for him to walk at night, though he did not show any increased swaying upon closing his eyes when his station was tested.

The pupils were equal and reacted normally. No nystagmus. The finger-to-nose test and the heel-to-knee tests showed some ataxia, but not nearly so much as might be expected. The deep reflexes of upper and lower limbs were all exaggerated.

His gait resembled somewhat that of a tabetic. The legs would be swung forward in the flail-like manner, but the toes would be held up and the knees would extend sharply, causing a peculiar bounding or springing effect. The arms would be held in extension backward, possibly as a partial balance, and the body flexed forward at the waist or hips. The arms jerked and the movements of the facial muscles would continue while the patient walked. While sitting, supposedly unobserved, the movements were not present, nor during sleep, and he could often stand quietly.

There were no sensory changes in either brothers. The sense of position may have been affected, as neither of them could use their hands very well, and they had great difficulty in eating and even in playing cards

Never any incontinence of urine or feces. Impotent for about ten years.

At intervals of a few seconds to a half-minute the patient would roll his eyes and close his eyelids and turn his head slightly, resembling somewhat a tic movement.

Case II.—D. D., aged forty-three years; farm laborer. Disease began about five years ago. Is a brother of Case I. Married and has five healthy children.

The symptoms in this case resembled very much those of his brother. His gait had more of the peculiar bouncing, mechanical character, and his condition is in general much further advanced.

In answering or attempting to answer questions the ataxia of the face and tongue was so extreme that he could not pronounce his name. In these attempts the mouth would be held open and the tongue could be seen rolling about in his ataxic effort to speak. All parts of his mouth could not be closed at once, so that his speech was often mumbling and indistinct. During his efforts he would hump his back and work his eyes and facial muscles.

The pupils reacted normally to light and accommodation. No nystagmus. Often the patient in trying to keep his eyes open would spasmodically close them. (In repose both brothers appeared to have ptosis.) Attempts to protrude the tongue would show great lack of control and ataxia; the patient would wag his tongue,

partially protrude it, and quickly pull it back, this continuing for four or five or more times before he could hold it out. The face could not be drawn up at the side voluntarily by either brother.

The deep reflexes were exaggerated but no Babinski. No sensory changes, either objective or subjective.

Finer movements, as in eating, etc., were impossible or most difficult.

Ataxia in knee-, heel-, and finger-to-nose tests was well marked. The patient could neither sit nor stand quietly. In this respect both patients resembled very much cases of Huntington's Chorea. Had incontinence of urine four or five times about ten years ago. He says his sexual power is not impaired.

CHOLESTERIN ANTIGENS IN THE WASSERMANN REACTION AND THE QUANTITATIVE TESTING OF SYPHILITIC SERA.

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AND

J. B. Zimmermann.

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1. Cholesterin Antigens. The addition of cholesterin to lecithin solutions or to alcoholic organ extracts used as "antigens" in the Wassermann reaction was first recommended by Browning, Cruickshank, and M'Kenzie, and later by Sachs, Walker and Swift, and others. The experience of all has been that such preparations give fixation of complement with many syphilitic sera which fail to react with similar extracts without the cholesterin. Walker and Swift tested the sera of twenty-two individuals in whom syphilis could reasonably be excluded with cholesterin-heart extract preparations and obtained no fixation except when an excessive amount of the extract was used, in which case some of the sera gave partial fixation. Recently, Thomas and Ivy have reported a number of false positive reactions obtained with these antigens. It should be noted, however, that they used only the minimal hemolytic dose of amboceptor and complement, a practice which of itself makes the test extremely sensitive and also unreliable, according to the experience of most workers.

The advantage of using antigens which will increase the number of positive reactions is obvious, providing there is reasonable certainty that the antigens will not react with non-syphilitic serum. However, some procedures which increase the delicacy of the reac-

tion, such as testing the serum without previous inactivation or using minimal amounts of complement and amboceptor, have been found to give non-specific reactions, and it seemed possible that such might be the case with the cholesterin antigens. For this reason we determined to test their sensitiveness and reliability by using them in a series of routine examinations, testing the same sera simultaneously with extracts possessing known properties.

The Wassermann reactions were carried out with one-half the original amounts: that is, 0.1 c.c. of patient's serum, 0.5 c.c. of diluted antigen, and usually 0.05 c.c. of guinea-pig serum (the exact amount being determined each day by preliminary titration) in the first stage, and 1 c.c. of 25 per cent. sheep cells sensitized with twice the minimal hemolytic dose of immune rabbit serum in the second stage. In testing spinal fluids 0.5 c.c. was used. Controls for anticomplementary action, one containing double the amount of serum (or spinal fluid) and one containing double the amount of antigen used in the test were always made. When the controls showed any inhibition the tests were disregarded.

The extracts were prepared by treating chopped moist guinea-pig heart with absolute alcohol for two to three weeks at 37° C., the proportions being 1 gm. of tissue to 10 c.c. of alcohol. To the filtered extract 0.4 per cent. cholesterin was added, and after this had stood for twenty-four hours in the incubator the undissolved residue was filtered off. This method is that recommended by Walker and Swift, except that guinea-pig heart was used instead of human. Emulsions for use in the tests were prepared by adding salt solution, at first drop by drop and then rapidly, to the alcoholic extract, the mixture being shaken during the process. A few tests were made with emulsions prepared in the reverse manner, the alcoholic extract being dropped into the salt solution, but the results seemed less satisfactory. Sachs and Rondoni found, in regard to simple alcoholic extracts, that dilutions made in the latter way were less anticomplementary but proportionately still less active as antigens, and consequently less satisfactory than the more turbid emulsions produced by the slow addition of salt solution to the extract. This has also been our own experience. The anticomplementary power of all the extracts was determined before use, and it was found that most of them produced slight inhibition in amounts from 0.1 to 0.12 c.c., but none in amounts of 0.08 c.c. or less. In performing the reactions one-fourth of the largest amount which showed no inhibition was used—usually 0.02 or 0.025 c.c.

In the control series of tests the acetone insoluble lipoids of beef-heart extract, prepared by Noguchi's method, were used as antigen.

The reactions obtained with sera from 475 patients and with 50 specimens of spinal fluid are shown in Table I.

partially protrude it, and quickly pull it back, this continuing for four or five or more times before he could hold it out. The face could not be drawn up at the side voluntarily by either brother.

The deep reflexes were exaggerated but no Babinski. No sensory changes, either objective or subjective.

Finer movements, as in eating, etc., were impossible or most difficult.

Ataxia in knee-, heel-, and finger-to-nose tests was well marked. The patient could neither sit nor stand quietly. In this respect both patients resembled very much cases of Huntington's Chorea. Had incontinence of urine four or five times about ten years ago. He says his sexual power is not impaired.

CHOLESTERIN ANTIGENS IN THE WASSERMANN REACTION AND THE QUANTITATIVE TESTING OF SYPHILITIC SERA.

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1. Cholesterin Antigens. The addition of cholesterin to lecithin solutions or to alcoholic organ extracts used as "antigens" in the Wassermann reaction was first recommended by Browning, Cruickshank, and M'Kenzie, and later by Sachs, Walker and Swift, and others. The experience of all has been that such preparations give fixation of complement with many syphilitic sera which fail to react with similar extracts without the cholesterin. Walker and Swift tested the sera of twenty-two individuals in whom syphilis could reasonably be excluded with cholesterin-heart extract preparations and obtained no fixation except when an excessive amount of the extract was used, in which case some of the sera gave partial fixation. Recently, Thomas and Ivy have reported a number of false positive reactions obtained with these antigens. It should be noted, however, that they used only the minimal hemolytic dose of amboceptor and complement, a practice which of itself makes the test extremely sensitive and also unreliable, according to the experience of most workers.

The advantage of using antigens which will increase the number of positive reactions is obvious, providing there is reasonable certainty that the antigens will not react with non-syphilitic serum. However, some procedures which increase the delicacy of the reac-

tion, such as testing the serum without previous inactivation or using minimal amounts of complement and amboceptor, have been found to give non-specific reactions, and it seemed possible that such might be the case with the cholesterin antigens. For this reason we determined to test their sensitiveness and reliability by using them in a series of routine examinations, testing the same sera simultaneously with extracts possessing known properties.

The Wassermann reactions were carried out with one-half the original amounts: that is, 0.1 c.c. of patient's serum, 0.5 c.c. of diluted antigen, and usually 0.05 c.c. of guinea-pig serum (the exact amount being determined each day by preliminary titration) in the first stage, and 1 c.c. of 25 per cent. sheep cells sensitized with twice the minimal hemolytic dose of immune rabbit serum in the second stage. In testing spinal fluids 0.5 c.c. was used. Controls for anticomplementary action, one containing double the amount of serum (or spinal fluid) and one containing double the amount of antigen used in the test were always made. When the controls showed any inhibition the tests were disregarded.

The extracts were prepared by treating chopped moist guinea-pig heart with absolute alcohol for two to three weeks at 37° C., the proportions being 1 gm. of tissue to 10 c.c. of alcohol. To the filtered extract 0.4 per cent. cholesterin was added, and after this had stood for twenty-four hours in the incubator the undissolved residue was filtered off. This method is that recommended by Walker and Swift, except that guinea-pig heart was used instead of human. Emulsions for use in the tests were prepared by adding salt solution, at first drop by drop and then rapidly, to the alcoholic extract, the mixture being shaken during the process. A few tests were made with emulsions prepared in the reverse manner, the alcoholic extract being dropped into the salt solution, but the results seemed less satisfactory. Sachs and Rondoni found, in regard to simple alcoholic extracts, that dilutions made in the latter way were less anticomplementary but proportionately still less active as antigens, and consequently less satisfactory than the more turbid emulsions produced by the slow addition of salt solution to the extract. This has also been our own experience. The anticomplementary power of all the extracts was determined before use, and it was found that most of them produced slight inhibition in amounts from 0.1 to 0.12 c.c., but none in amounts of 0.08 c.c. or less. In performing the reactions one-fourth of the largest amount which showed no inhibition was used—usually 0.02 or 0.025 c.c.

In the control series of tests the acetone insoluble lipoids of beef-heart extract, prepared by Noguchi's method, were used as antigen.

The reactions obtained with sera from 475 patients and with 50 specimens of spinal fluid are shown in Table I.

TABLE I.

Condition.	Number of cases.	Lipoid antigen. Number of positive reactions.	Cholesterin antigen. Number of positive reactions.
Blood-serum:			
Primary syphilis	10	6	7
Secondary syphilis	25	21	25
Tertiary syphilis	99	59	79
Congenital syphilis	9	5	7
Tabes dorsalis	20	9	13
General paresis	4	4	4
Latent or cured syphilis	44	17	29
Apparently non-syphilitic	264	4	25
Spinal fluid:			
Tabes dorsalis	19	8	10
General paresis	3	3	3
Tertiary syphilis	9	3	2
Non-syphilitic	19	0	1

In tabulating our results we have recorded as positive only those of the tests which showed no or very slight hemolysis after an hour's incubation in the second stage. When using the lipoid antigens all tests showing 50 per cent. or less hemolysis may safely be called positive, and such readings would give a somewhat larger proportion of positives with these antigens in luetic cases than the table shows. Many non-luetic sera, however, gave partial inhibition of hemolysis with the cholesterin-heart extract preparations, and better results were obtained with these if only those sera which caused practically complete inhibition were regarded as positive.

The cases are grouped in the table according to the clinical diagnosis. Many cases which seemed doubtful have been disregarded; but, even so, the probability of some errors in diagnosis must be considered before conclusions are drawn from these figures. One difficulty is that the diagnosis in many cases was doubtless influenced by the result of the Wassermann reaction. As a matter of fact, cases giving an indefinite history of lues with a positive serum reaction have been included under the head of "latent syphilis," whereas cases giving a negative reaction were not considered to be syphilitic unless the history or clinical picture was fairly characteristic of the disease.

Of the 525 reactions which have been included in the series the result was the same with both types of antigen in 455. Only two specimens which were positive with the "lipoid" antigen were negative with the "cholesterin." These were both spinal fluids, one from a case of tabes and one from a case of cerebrospinal syphilis. On the other hand, 68 specimens reacted positively with the "cholesterin" antigen, but not with the "lipoid;" of these cases 46 were syphilitic and 22 apparently non-syphilitic. Of the former, 3 were treated secondary cases and 1 an untreated secondary; but the majority were tertiary or latent cases. Of the 26 which have been classed as non-syphilitic, 1 was a case of sarcoma, 4 were cases

of carcinoma, and 4 cases of pernicious anemia. One was a case of estivo-autumnal malaria; a condition in which positive Wassermanns have frequently been reported. The other cases represented a variety of conditions, many of them local infections; but except for the cases mentioned these false positive reactions were not found twice in the same disease, and there seems no reason to believe that the illness of the patient at the time was responsible for the result of the test. The Wassermann reactions were not made as a routine on all admissions, so that in nearly all these cases which we have classed as probably non-syphilitic the possibility of lues was considered at the time the tests were made. In several instances, however, the nature of the suspected gumma or ulcer was determined by histological examination; and in the remainder, further observation ruled out syphilis so far as the present illness was concerned. It is, however, impossible absolutely to exclude latent syphilis in these cases. Four cases that were clinically non-luetic gave reactions with both types of extracts used. It is certain that the "lipoid" antigens rarely, if ever, give false positive reactions, and it is probable, therefore, that these patients had unrecognized infections. It seems highly improbable, however, that 25 out of 264 patients, or 9 per cent., presenting no history or signs of syphilis, should in fact be luetic.

A factor which probably accounts for some of our non-specific reactions is the instability of these extracts. A number of the false positive tests were obtained with a preparation which was over six weeks old. At this time it was found that the anticomplementary power had increased very considerably, and although the amount used in the reaction was proportionately decreased, a number of positive tests which could not be explained by the clinical data were obtained. In view of this experience, antigens less than four weeks old only were subsequently used, with considerable improvement in the results. As the presence of a slight excess of antigen also seems to produce non-specific reactions the making of an anticomplementary control containing four times instead of twice the amount of antigen used in the test is recommended.

In spite of the apparently false reactions obtained, we believe that these extracts are of distinct value on account of the large number of positive results obtained in tertiary syphilis and in cases cured so far as symptoms were concerned, which failed to react with the "lipoid" antigens. There are obvious advantages in so sensitive a test in controlling treatment, or in cases where it is desired to exclude syphilis so far as possible, as, for example, in selecting donors for blood transfusion or in examining wet-nurses. The reactions are also very helpful in diagnosis when there is some clinical evidence in their support.

It should be remembered, however, that the nature of the Wassermann reaction is not known and that it is essentially empirical.

Until it can be shown by long experience, therefore, that these extracts do not react with non-luetic sera they should not replace extracts whose reliability has been established. What evidence we have been able to obtain indicates that they do give complement fixation with some non-syphilitic sera. It would seem advisable, then, in routine work to test all sera both with a sensitive cholesterin preparation and with some less sensitive but thoroughly reliable extract.

2. THE QUANTITATIVE TESTING OF SYPHILITIC SERA. Another phase of the Wassermann technique which has interested us has been the determination of the strength of the reaction in positive sera. This is specially important in following cases under treatment. The most logical method is to make tests with various amounts of the serum, to determine how small an amount will produce the reaction. In order to measure the small amounts required at least two preliminary dilutions of each serum to be tested must be made, and this very considerably increases the labor of carrying out a large series of reactions. In some laboratories this difficulty is avoided by testing constant amounts of serum against serial dilutions of the antigen, which can be prepared in bulk for all the tests to be made on a given day.

A technique based on this principle was introduced by Coca and l'Esperance, and in their hands gave excellent results, and we have followed their procedure with slight variations in making some five hundred Wassermann tests. The reaction is carried out with one-tenth the volume used in the original Wassermann method. The patient's serum (unheated) is first diluted with four parts of salt solution, and 0.1 c.c. is placed in each of five tubes; in a sixth tube 0.2 c.c. is placed for a control. As antigen a 2 per cent. solution of the acetone insoluble fraction from normal beef-heart extract prepared by Noguchi's method is used. Emulsions are prepared containing 0.05, 0.025, 0.012, 0.006, and 0.003 c.c. of this stock solution per cubic centimeter, and each serum is tested with 0.1 c.c. of each of these dilutions; $\frac{1}{10}$ c.c. of a 1 in 10 dilution of guinea-pig serum is used in the test, with 0.1 c.c. of a 5 per cent. emulsion of sheep corpuscles and two units of hemolytic amboceptor.

The use of the patient's serum without previous inactivation is thought by some workers to be a safe procedure, provided that antigen free from protein constituents is used, although it is admitted that false positives are obtained with simple alcoholic organ extracts. Although in our tests a carefully prepared "lipoid" antigen was used, positive reactions were obtained in a few cases in which there was no evidence of syphilis other than this reaction, and in which the inactivated sera were negative both with "lipoid" and with "chloesterin" antigen. While some sera from tertiary and latent cases reacted positively in fresh condition, but not when inactivated, four sera which when active gave negative results, after inactivation

TABLE II.—Estimates of Strength of Sera Obtained by Various Methods, Compared.[1]

	(a) Sera tested in graded amounts against 0.02 c.c. of lipoid antigen.					(b) Sera tested in graded amounts against 0.05 c.c. of cholesterin antigen.					(c) Same sera tested in constant amounts (0.1 c.c.) against graded amounts of lipoid antigen.					(d) Same sera tested in constant amounts (0.1 c.c.) against graded amounts of cholesterin antigen.				
	Amount of patient's serum.					Amount of patient's serum.					Amount of antigen.					Amount of antigen.				
	.1	.05	.025	.0125	.0062	.1	.05	.025	.0125	.0062	.02	.01	.005	.0025	.00125	.05	.025	.0125	.0062	.0031
1. Secondary	0	0	0	++	++++	0	0	0	+++	++++	0	0	0	0	0	0	0	0	0	0
2. Tertiary	++	++	++++	++++	++++	0	0	+	++++	++++	++	++++	++++	++++	++++	0	0	0	0	0
3. Tertiary	0	0	0	0	+	0	0	0	0	0	0	0	+	++	+++	0	0	0	0	+
4. Tabes	0	0	0	+	++++	0	0	0	++++	++++	0	0	0	0	0	0	0	0	0	0
5. Secondary	0	0	0	+++	++++	0	0	+	++++	++++	−	0	0	0	−	0	0	0	0	0
6. Latent	0	0	0	++	++++	0	0	+++	++++	++++	0	0	0	+++	++++	0	0	0	0	0
7. Tertiary	0	0	0	++	++++	0	0	0	+	++++	0	0	0	0	++	0	0	0	0	0
8.	0	+	++++	++++	++++	0	0	+++	++++	++++	0	0	+	++++	++++	0	0	0	0	0
9. Latent	0	0	0	++	++++	..	..	..	....	....	0	0	0	0	0					
10. Latent	0	0	0	0	0	..	..	..	....	....	0	0	0	0	0					
11. Latent	0	0	0	0	+	..	..	..	....	....	0	0	0	0	0					
12. Tertiary	0	0	0	0	+	..	..	..	....	....	0	0	0	0	0					
13. Tertiary	0	0	++++	++++	++++	..	..	..	....	....	0	0	0	0	++++					
14. Tertiary	0	0	0	++	++++	..	..	..	....	....	0	0	0	0	0					

0 = no hemolysis.

++++ = complete hemolysis.

[1] The cholesterin antigens in this experiment were in clear emulsion, obtained by adding the extract to the diluent drop by drop. Consequently, relatively large amounts were used.

gave positive results with the same antigen. These negative reactions were probably due to the complement in the patient's serum. The results make the employment of active serum appear distinctly disadvantageous. Moreover the small quantities used in this technique introduce the possibility of error on account of the care required to deliver 0.1 c.c. accurately from the blunt-tipped pipettes which are usually employed in this work.

The method was chiefly interesting, however, as a means of determining the strength of the reaction. The majority of the sera which reacted at all gave complete inhibition in at least four of the five tubes set up. For example in tertiary cases, where weaker reactions would be expected, out of 60 positive sera, 27 reacted in the fifth tube containing one-sixteenth of the usual amount of antigen, and 41 reacted in the fourth tube of the series. As so many specimens reacted alike the method did not give a very satisfactory grading of their strength. A series of higher dilutions would doubtless have brought out further differences. It has been asserted by MacIntosh and Fildes that titration with varying amounts of antigen does not give an accurate estimation of the strength of the reaction. They base this assertion on experiments in which the same sera were titrated, using varying amounts of serum with constant amounts of anitgen, and also using constant amounts of serum with varying amounts of antigen. We tested in this way fourteen sera, using the "lipoid" type of antigen, and eight with the "cholesterin" type also, as shown in Table II.

The titrations in which the amount of serum was graded (*a* and *b*, Table II) with both antigens showed considerable variations in strength among the sera used. When titrated in the reverse way with the less sensitive antigen (*c*) the relative values did not run parallel, and the differences between them were much obscured; while with the more sensitive antigen (*d*) these differences were lost almost altogether.

It seems then that a closer estimate of the strength of syphilitic serum may be obtained by determining how small a quantity of it will produce a reaction, rather than by determining with how small an amount of antigen it will react; or, in other words, that quantitative Wassermann tests should be made by varying the amount of serum used, and not the amount of antigen.

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AN UNATTACHED MASS FOUND IN THE ABDOMINAL CAVITY OF A MALE.

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Inasmuch as the following case report is extraordinary, it is of interest, but insofar as it raises the question of intra-abdominal growth without obvious nourishment, it is perhaps of more scientific importance. It is, therefore, best to leave any discussion until the facts are portrayed.

A. McL., aged sixty-nine years, was admitted to the Montreal General Hospital November 10, 1912. He had suffered from digestive disturbances for forty years, more or less, complaining chiefly of constipation, a burning sensation in the stomach after eating, and of distention and discomfort from gas in the bowels. There was no nausea or vomiting. Two or three years ago he had attacks of pain in the region of the appendix, which called on one occasion for morphin. He did not vomit in these attacks.

For a period of about twenty-five years he can remember a mass in the right side of the abdomen, which at first was quite small, smaller than a hen's egg, and was always freely movable, so movable that it would disappear, apparently into the pelvis, for two or three days at a time. He could push it into any part of the abdomen he wished, but it was first found in the right hypochondrium, and he was most comfortable when it remained in that situation. It always tended to follow the laws of gravity, and in consequence was generally to be found in the most dependent part of the abdomen, falling from side to side as he turned in bed. He had the impression that it was a floating kidney, and indeed he had been told by his medical advisers that this was the most probable diagnosis. The urine, however, had until recently never shown any pathological changes, nor had he suffered any renal crises. He had had pain in the region of the right hypochondrium of a more or less indefinite nature.

We had an opportunity of discussing the case with his physician, who had noted the mass when he first examined him six years previously. It was then the size of a large hen's egg, and of the present consistence. It had, to his certain knowledge, increased

in size to its present dimensions, which may be described as those of a large orange or a small grapefruit.

The patient came to the Montreal General Hospital on account of an attack of cystitis, with retention, which he had developed in consequence of an hypertrophied prostate gland.

On examination he was found to be a spare, rather pale old man, with little or no subcutaneous fat; arteries moderately sclerosed; normal lungs and heart; rather anemic, and altogether frail. His urine contained considerable pus, and he suffered almost complete retention, due to a moderately hypertrophied prostate gland.

The abdomen was scaphoid, the umbilicus prominent, and the walls soft and non-resistant, making palpation easy. In the right upper quadrant was a hard, slightly irregular mass the size of a large orange. This could be turned about so as to present slightly different aspects to the examining hand, could be pushed downward, and even across the spine to the left side without any trouble, and would stay where placed. It was too large to go down into the pelvis, but this was the only apparent reason why it should not do so, it was so freely movable.

An *x*-ray examination gave no shadow. It was not tender. It was dull on percussion, and was evidently situated in front of the bowels. It was not kidney, but the kidneys were not palpable. The two most marked features about it were its extreme mobility and its marked hardness. The diagnosis of an omental tumor was made.

Operation.—The patient was not a good operative risk, owing to the infection of his urinary tract, which apparently involved the kidneys. He was, therefore, put upon catheter life, with daily bladder lavage. So anxious was he, however, that something should be done for the abdominal condition, and so simple did the operation appear, that on November 18, 1912, under gas and oxygen anesthesia, the abdomen was opened directly over the mass, which had to be held stationary by an assistant. In cutting through the peritoneum, we came at once upon the tumor, which showed a pearly white glistening surface, exactly comparable to a uterine fibroid. Pressure on either side of the wound caused the mass to pop out of the wound on to the abdominal wall. It had absolutely no pedicle, nor any attachment whatever. It bore no apparent relation to any viscus, nor was there an adhesion of any kind attached to it. Indeed, on searching the abdomen there did not seem to be any adhesions present. There was, however, a small amount of fluid about the loops of small bowel. The wound was closed, and the patient did well for the next seven or eight days, when he began to fail, with frequent attacks of vomiting and hiccough. The wound, however, remained normal, and it was evident that the lesion was outside the peritoneal cavity. He died January 6, 1913, forty-eight days after the operation.

The autopsy protocol is as follows:

Montreal General Hospital, 13.8, January 7, 1913. Ten hours postmortem.

The body is that of a poorly developed, much emaciated male adult. No edema is present, but considerable lividity of the dependent parts. Rigor mortis is marked.

Abdomen. There is an elevated bluish scar in the middle line, between the umbilicus and the ensiform cartilage, 13 cm. in length (operation wound).

Peritoneal Cavity. The peritoneal cavity shows no excess of fluid. The peritoneum is smooth and shiny, but darkly pigmented on both parietal and visceral layers. Mesentery is bluish-black. Mesenteric glands are slightly enlarged and darkly pigmented. There are extensive general fibrous adhesions in the abdominal cavity between the liver and colon, the spleen and colon, and binding down the cecum to the posterior abdominal wall. The appendix is retrocecal, surrounded by fibrous adhesions. In one of the fibrous adhesions between the transverse colon and the under surface of the left side of the diaphragm is found a hard calcified mass 0.5 cm. in diameter. It is not attached to the mesentery. A similar mass, perfectly spherical, measuring 0.7 cm. in diameter, is found under the peritoneum of the small bowel about 36 inches above the ileocecal valve. This body is white and calcified, with a smooth surface under glistening peritoneum, and is 2 cm. from the mesenteric attachment (Fig. 1).

Pleural Cavity. This contains no excess of fluid, but there are extensive fibrous adhesions on both sides.

Pericardial cavity. The pericardial cavity contains no excess of body fluid. There are extensive adhesions, delicate and recent, and firm and old between both layers of the pericardium.

Heart. The heart is 320 gm. in weight. It is pale brown on section, and the muscle is soft. The endocardium is normal. The aortic arch shows some raised whitish discoloration. The coronary arteries are patent and show a moderate degree of atheromatous change.

Lungs. The right upper and lower lobes are full and firm to the touch. On section they are of a general grayish, mottled appearance. There are many raised gray areas alternating with edematous lung tissue. Even on gentle pressure, much pus and purulent fluid exudes from these areas. The right middle lobe is dark red in color and edematous. The upper and lower lobes are nodular and uneven to the touch. The lower lobe on the left side presents a similar condition to that of the upper and lower lobes on the right side. There are several old pleural scars at the apices of both sides, but no calcareous or caseous nodules are found.

Spleen. Normal.

Stomach. Normal.

Intestines. Normal.

Pancreas. Normal.

Liver. Weight, 1580 gm. It shows on the under surface of the right lobe, retroperitoneally, an area 10 x 6 cm., which forms one of the confines of the large, perinephritic abscess described below. Otherwise the organ shows nothing abnormal.

Kidneys. The right kidney weighs 300 gm. There is a perinephritic abscess cavity connected with the upper pole of the kidney, and extending upward to the liver. This cavity measures 12 x 6 x 10 cm., and is filled with a greenish-brown purulent fluid. The right kidney shows extensive abscess condition throughout. The right ureter is thickened, and the mucous membrane is red

FIG. 1.—Small subperitoneal calcareous nodule found in the small bowel.

and granular. The left kidney is more normal. The cortex averages 0.3 cm. in thickness. The capsule strips with difficulty, and leaves an uneven surface, which shows some retention cysts. The vessels are tortuous. There is no sign of infection.

Right Adrenal. The right adrenal cannot be found, but the left is normal.

Bladder. The bladder is much thickened and trabeculated, with a pigmented and granular mucosa.

Prostate. The prostate is large.

Aorta. The aorta shows marked atheromatous degeneration, especially about the origin of the intercostals.

ANATOMICAL DIAGNOSIS. Pyonephrosis; perinephritic abscess (right); acute and chronic pericarditis; bronchopneumonia; chronic cystitis; chronic nephritis; calcified nodules, subperitoneal; hypertrophied prostate.

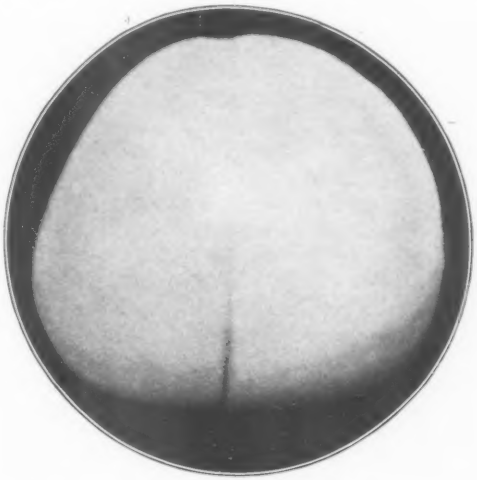

FIG. 2.—View of the mass as removed from the abdominal cavity, about two-thirds actual size.

FIG. 3.—View of mass on section, showing calcareous centre, but not the concentric arrangement of layers.

HISTOLOGICAL EXAMINATION. Montreal General Hospital, S., 12, 635, November 18, 1912.

The tumor is roughly spherical in shape, but with three flattened surfaces or facets (Fig. 2). It measures 9 x 8 cm. in diameter, and has a smooth, white, glistening surface, without pedicle or any adherent tissue. It is very firm. On section, the mass cuts with some difficulty, and is seen to have a calcareous centre, 1.5 cm. in diameter (Fig. 3). The sectional surface is, for the most part, white and very firm, but an occasional darker ring or lamella accentuates a concentric formation, which is evident in both diameters. The tissue immediately around the calcareous centre is somewhat softer than the remainder.

Sections cut from the mass in various regions show a tissue composed of laminated branching fibers, which take a homogeneous color with methylene blue, and the various differential stains employed. No vessels, cells, nuclei, or fibrils can be demonstrated. In the centre of some fibers, a fine granular deposit is noted, probably calcium salts.

To establish the identity of the tissue is difficult. Were it the remains of a true fibroma, one would expect evidences of vessels, or at least spaces, to persist. The question arises whether it is simply fibrin which has been deposited, layer after layer, on whatever originally was the nucleus, or whether it is collagen remaining from organization of layers of fibrin, similarly deposited by fibroblasts, which have subsequently disappeared, leaving resistant collagen lamellæ.

The tissue takes a homogeneous blue stain with Mallory's connective-tissue stain, and pink with phosphotungstic acid hemotoxylin. These are the reactions for collagen. To try and further rule out fibrin, an attempt was made to digest the tissue with pepsin, controlled by the digestion of fresh fibrin, and formalin fixed fibrin (the tumor tissue having been fixed in formalin), but neither the formalin-fixed fibrin nor the tissue fibers were digested.

Certain facts seem worthy of reiteration:

1. The tumor had been present twenty years or more, and had been noted by the patient's present physician six years ago.
2. It had always been freely movable.
3. It had never caused pain, other than a feeling of discomfort from moving about.
4. It had grown steadily and slowly from a small nodule, which frequently disappeared for days, to a tumor too large to enter the pelvic inlet.
5. Operation showed it to be absolutely unattached, either by pedicle or by a surrounding envelope of omentum or adhesion.
6. There is no evidence that a pedicle was ever present.
7. Postmortem examination of the abdomen showed one calcareous nodule on the small bowel, which was, however, entirely

covered by peritoneum, and another surrounded by adhesions in the neighborhood of the large bowel.

8. The centre of the mass was calcareous.

9. Section of the tumor showed that about this calcareous centre were concentric rings (in three dimensions), similar to those seen about the nucleus of a vesical calculus.

10. Microscopically, the tumor consists of a homogeneous tissue arranged in concentric layers, the exact nature of which cannot be determined, but which probably are either fibrin or organized fibrin, with disappearance of the cellular elements.

As to the origin of the tumor, the following explanations seem worthy of discussion.

1. The tumor may represent a pediculated fibroid or fibroma, which was originally attached to some viscus, or to the abdominal parietes, and became detached, calcified in the centre, and remained a foreign body in the peritoneal cavity. The entire absence of any sign of pedicle, not only on the surface, but in the outline of the concentric rings, vitiates this hypothesis.

2. A calcareous mass similar to those found at autopsy, or indeed a small fibroma in such a situation, might have gradually grown by having new layers added to it from the surrounding envelope of peritoneum, until reaching a certain definite size, its mere weight, or accident tears a way through the peritoneal covering, leaving it a free body in the abdominal cavity.

3. The small tumor or nodule, freed from its attachment in the above manner, may have continued to grow within the abdominal cavity, much as a pearl does in the shell of an oyster, causing a certain irritation of the peritoneum, and an outpouring of fluid and cells (there was definite fluid present). The coagulation of fibrin over the offending surface and the gradual organization of the same might follow. The definitely recurring layers are in favor of some such view.

4. A combination of the second and third is, of course, another possibility, and is perhaps the most likely. That is to say, the earliest growth took place subperitoneally or elsewhere, and the later growth, while it was a free body in the peritoneal cavity. Calcification may have occurred at any time.

We have been unable to find any report of a similar case, though it is quite possible that such may have escaped our notice, owing to the difficulty of classifying an unusual condition in the literature.

Fibromas of the abdominal parietes and contents have been noted, but are not common. The instances recorded do not seem to throw any light upon the present case.

THE VALUE OF PETECHIÆ IN DIAGNOSIS AND PROGNOSIS.

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Every case of doubtful diagnosis should be thoroughly inspected for evidences of hemorrhagic lesions. In the routine examination of a patient, an enlarged spleen, a cardiac murmur, or an abnormal abdominal mass are seldom overlooked; but a subconjunctival hemorrhage or a crop of petechiæ around the knee are just as seldom observed. The finding of a minute petechia on the mucous membrane of the palate or in the conjunctiva will not definitely establish a correct diagnosis, but it will, by eliminating the many conditions in which these hemorrhages are absent and by furnishing a positive sign which we cannot discard, serve as a great aid in the solution of the problem.

The idea in mind in writing this paper is not to compile an exhaustive treatise on the hemorrhagic eruptions, but to mention several unusual cases in which the occurrence of petechiæ afforded a clue to the proper diagnosis or was striking on account of its rarity in these cases. A summary in the beginning, of the common conditions in which we are likely to find petechiæ, should not be irrelevant. They are as follows:

1. Acute Infectious Diseases. Any bacteriemia may develop petechiæ, as pneumonia, bacterial endocarditis, postpartum or post-traumatic sepsis, in which cases the hemorrhages may be embolic in origin. This may be likewise true in cases of pernicious malaria, many of which are accompanied by a petechial eruption; in some of these cases thrombi produced by masses of bacteria have been found in the brain at autopsy. Under the heading of acute infections we may also classify those diseases in which there is not a general systemic infection or at least in which our present laboratory methods are insufficient to establish a bacteriemia, as in yellow fever, most cases of cerebrospinal meningitis, and the acute exanthemas, as scarlet fever, measles, and smallpox.

2. Toxic States not Associated with or Secondary to Bacterial Infectious Agents. In this category as causative factors are:

(*a*) *Drugs:* As quinine, copaiba, belladonna, potassium iodide, alcohol, ergot, chloral, salicylic acid, and benzine vapor.

(*b*) *Urinary Sepsis:* In uremia or after operative procedures upon the urinary tract, where the patient is overpowered by the toxins due to a suppression or retention of urine, petechiæ are not uncommon.

(*c*) *Snake-bite.*

(*d*) *Jaundice.*

In the latter two conditions there is often a general hemorrhagic tendency evidenced not only by purpura, but in many instances by extensive subcutaneous extravasations.

3. Blood Diseases. Practically all the blood diseases may show at some time a more or less extensive petechial eruption, as leukemia, pernicious anemia, etc. Under this heading, or under that of the acute infectious diseases, we may classify the simple and the so-called "rheumatic" purpuras, the Henoch's and Schönlein's type, and the "erythema group" of Osler's, in which hemorrhagic lesions are characteristic.

4. Conditions Produced by Mechanical Causes. Sudden changes of atmospheric pressure, as in caisson disease, or paroxysms of coughing, as in pertussis, or convulsions of any kind, are likely to be associated with hemorrhages.

5. Exhaustive States. Carcinoma, tuberculosis, Hodgkin's disease, and other wasting illnesses in their last stages are known to produce petechial and other hemorrhagic lesions.

6. Nervous Diseases. Both organic diseases, as myelitis and tabes dorsalis, and functional conditions, as hysteria, are occasionally associated with skin hemorrhages.

Petechiæ in bacterial endocarditis, in Henoch's purpura in epidemic cerebrospinal meningitis, and in the bacteriemias of pyogenic origin are not uncommon. I shall take occasion, therefore, to cite only unusual cases, which I observed recently while in charge of the admitting department of the Mt. Sinai Hospital, in which petechiæ played an important part in the diagnosis.

Case I.—*History of erysipelas followed in two weeks by high fever and prostration; petechiæ in conjunctiva; diagnosis of streptococcemia made; Bacillus typhosus in blood culture.*

C. Z., aged thirty-six years. (Service of Dr. Rudisch.) The past history was negative. There were no infectious diseases. Four weeks before admission the patient had been treated for erysipelas of the leg, which had run a mild course, and had apparently been cured in about a week. For the two weeks prior to admission there had been gradually increasing headache, fever, malaise, and shortness of breath. On admission the patient appeared mildly prostrated. Evidences of the former erysipelas had entirely disappeared. The temperature was 103° and the pulse 110. In the left lower conjunctiva were three distinct petechiæ, in the right, one. The remainder of the physical examination was negative. The spleen was not felt; the pulse was not dicrotic; there was no eruption. The diagnosis of bacteriemia secondary to the previous erysipelas was made. The day after admission fresh petechiæ were found in both conjunctivæ. The blood-count showed a slight leukocytosis, with 66 per cent. of polynuclear leukocytes, 33 per cent. of lymphocytes, and 1 per cent. of transitionals. The temperature ranged between 103° and 105°. Four days after

admission the spleen became palpable. The blood-culture taken the day of admission was reported positive, not for the Streptococcus pyogenes or staphylococcus, as was expected, but for the Bacillus typhosus. The patient became more and more prostrated. Several days after admission there were evidences of intestinal hemorrhage; a week later perforation of the bowel occurred, resulting in death, despite the early diagnosis and immediate operation.

A search of the literature fails to show many cases of typhoid fever with petechiæ on record. In fact, the one distinguishing sign which differentiated typhoid and typhus fever in the days when the latter disease flourished was the presence of petechiæ in typhus. This must be considered, therefore, as a rather unusual case.

CASE II.—*Acute onset with fever, vomiting, and convulsions, in a child; signs of meningitis; skin petechiæ; no meningococci in spinal fluid; recovery; acute polioencephalitis.*

J. B., aged five years. (Service of Dr. Koplik.) The child had been well up to four days prior to admission, at which time the patient had become acutely ill with fever and headache. He had vomited once at the onset. Just before the child was brought to the hospital he had had a general convulsion lasting ten minutes. Physical examination revealed a condition of semistupor, a temperature of 104°, a slight Macewen sign, a tâche cérébrale, a Babinski reflex on the right side, and a Brudzinski sign. On the skin over the right deltoid were five or six small but definite, apparently recent, petechiæ. There was no rigidity of the neck; there were no palsies. The diagnosis of epidemic cerebrospinal meningitis was made. The next day the following data were obtained: Blood-count, 18,200 white blood cells, with 85 per cent. polynuclear leukocytes and 15 per cent. lymphocytes. On lumbar puncture, 12 c.c. of clear fluid under pressure was obtained, the cytology of which was later reported to be 100 per cent. lymphocytes. No tubercle bacilli were found. Four days afterward a facial palsy became apparent, and the next day decided weakness of the right leg. The stupor was somewhat less marked, but the other signs of meningitis seemed to be on the increase. Within twenty-four hours, however, the symptoms abated, the palsies lessened, the petechiæ disappeared, and the patient steadily improved until his discharge three weeks later, at which time he had fully recovered.

That polioencephalitis and meningitis are not easily distinguishable in many cases is a matter of common knowledge. It is, therefore, rather unfortunate for the science of diagnosis that the classical sign of cerebrospinal meningitis, the sign that caused it to be known as spotted fever, and upon which the diagnosis has often been made, should be usurped by another condition so analogous in its manifestations.

CASE III.—*Acute lobar pneumonia; jaundice; pneumococcic sepsis; petechiæ.*

J. B., aged thirty-eight years. (Service of Dr. Manges.) The patient's present illness began six days before entering the hospital, with a chill, fever, and pain in the right side of the chest. Later a slight cough developed. All symptoms increased to the time of admission: The examination on admission revealed signs of a lobar pneumonia on the right side, extending almost to the spine of the scapula. The patient showed evidences of marked prostration. There was a double mitral murmur, but no signs of cardiac decompensation. Jaundice appeared soon afterward and steadily progressed. One week after admission several crops of petechiæ were observed over both shoulders. The blood-culture taken at this time showed the pneumococcus. The patient's general condition became gradually worse, and he died two days later.

In this case, although it is conceivable that the petechiæ may have been dependent upon the jaundice, it is more probable that they were due to the pneumococcemia. Petechiæ in pneumonia, even without a demonstrable bacteriemia, may occur, although these cases are not common. An analogous case, also on the service of Dr. Manges, I reported about six months ago. Here, however, the diagnosis presented some difficulty, from the fact that the petechia was in the conjunctiva and minutely resembled those characteristic of bacterial endocarditis.

CASE IV.—*Emaciation; marked anemia; conjunctival petechiæ; admitting diagnosis: pernicious anemia; blood-count typical of lymphatic leukemia.*

E. S., aged forty-six years. (Service of Dr. Brill.) This patient gave a history of a rather vague onset, two months prior to admission, of epigastric cramps and anorexia. These symptoms continued with, in addition, a steady decline in weight. Excessive thirst was the patient's chief complaint. There was no vomiting, no polyuria, no bleeding from any mucous membrane. On admission the patient looked anemic, and showed evidence of marked emaciation and asthenia. The tongue was extremely dry and rather beefy in its appearance. The liver was enlarged to two fingers below the free border of the ribs. There were no glands or spleen to be felt. The reflexes were somewhat exaggerated. In both lower conjunctivæ there were several small but definite petechiæ. There were three possibilities considered at the time of admission: diabetes, eliminated by the negative result of the urinary examination, malignancy, and a blood disease. The last diagnosis was finally decided upon, and the patient admitted to the wards with the working diagnosis of pernicious anemia, no blood-count, however, having been taken in the admitting department. On the wards the blood-count was shown to be 40,000 white blood cells; small lymphocytes, 54 per cent.; large lympho-

cytes, 44 per cent.; polynuclear leukocytes, 2 per cent.; and hemoglobin, 42 per cent. Three days afterward petechiæ were seen on both arms. Later, diarrhea and weakness became marked, the skin hemorrhages increased greatly in number, and the patient finally died about three weeks after admission. At no time were there glands or a spleen to be felt.

In this case, although, of course, the petechiæ did not determine the diagnosis, they were, taken together with the anemia, instrumental in limiting the diagnosis to that of a blood disease. The exact type of blood disease was of secondary importance at the original examination. In several other cases of leukemia seen recently the diagnosis was suggested by the presence of skin and subconjunctival petechiæ, enlarged glands, and a palpable spleen having been absent.

CASE V.—*Signs of purpura hemorrhagica; steady progression of symptoms; ulcerations and gangrene; fatal outcome.*

H. A., aged fourteen years. (Service of Dr. Manges.) The past history was negative, with the exception of frequent attacks of tonsillitis. Six weeks before her appearance at the hospital, after exposure, the patient felt chilly, and complained of general aching pains and a soreness and redness of the left eye. These symptoms abated in a few days, but recurred five weeks later, accompanied by pain in the right wrist and knee. The day before admission the swelling of the right wrist and knee became aggravated, and was accompanied by a chill, considerable fever, and the appearance of a moderate number of small red spots in the skin around the swollen joints. On admission the patient looked acutely ill and in severe pain. Both wrists, ankles, and knees were swollen, red, and tender to the touch. Around several of the joints, in the conjunctivæ, and on the abdomen, were petechiæ, some minute, others as large as the head of a pin; on the buttocks were two somewhat larger hemorrhagic areas. The subsequent course of this patient presented a picture never to be forgotten. Daily, almost hourly, fresh hemorrhages occurred on the chest, abdomen, legs, buttocks, and in the mouth. All of these steadily underwent the same transformation. The hemorrhages would increase in size to that of a ten-cent piece or even a quarter, then develop around their periphery an inflammatory red zone, begin to ulcerate, become foul-smelling, gangrenous, and finally slough away. Despite all methods of treatment this process of destruction continued to increase, until just before death one-third of the skin of the body and of the mucous membranes of the mouth, larynx, rectum, and vulva was involved. The patient died three weeks after admission.

This case has been reported on account of its rarity. The simple purpuras, the rheumatic purpuras, and those associated with visceral manifestations usually have an excellent prognosis. It

is uncommon to see a case of this description, manifestly rheumatic in etiology, resist all therapeutic measures and terminate fatally.

CASE VI.—*Case of myocarditis and nephritis; Bacillus coli communis pyelitis; petechia in conjunctiva; sudden death.*

G. B., aged forty-nine years. (Service of Dr. Rudisch.) The patient gave the usual history of a cardionephritic case; dyspnea, slight edema of the legs, and cough for many months. Several days before admission the swelling of the legs had increased considerably, and the urine had become scanty. There had been slight fever and occasional sweats; no chills. Examination revealed the clinical signs of myocarditis, with nephritis, dyspnea, pulmonary congestion, weak heart sounds, swollen liver, and edematous legs. Besides this, there was found in the left lower conjunctiva a distinct petechia. The urine showed considerable albumin, pus, red blood cells, and many casts. Culture of a catheterized specimen showed the Bacillus coli communis. The petechia disappeared within forty-eight hours. The patient gradually improved and had been out of bed for several days, when he was suddenly seized with a convulsion, followed by almost immediate death.

Similar cases are not uncommon. One analogous case was seen recently on the service of Dr. Brill, where the lower extremities of a nephritic patient were almost covered with minute petechiæ. It is conceivable that these small hemorrhages may be the result of increased blood-pressure or may be evidences of a toxemia. In favor of the latter theory may be mentioned instances of petechiæ in those cases of so-called urinary sepsis following kidney or prostate operations, where the system is poisoned by an accumulation of toxins unable to be eliminated by the usual channel.

CASE VII.—*History of a debauch; conjunctivitis; numerous petechiæ in upper and lower conjunctivæ.*

A. B., aged twenty-seven years. This patient was seen twelve hours after a night of dissipation. He was unaccustomed to the frequent use of intoxicating liquors. Six months before, a similar debauch was followed by the same symptoms. There was evidence of a mild conjunctivitis. In the upper and lower conjunctivæ of both eyes were seen many petechiæ of varying sizes, not merely dilated bloodvessels, but actual hemorrhages into the tissues. Seventy-two hours elapsed before the absorption of these hemorrhages.

It is interesting to note that the toxic effect of the alcohol in this case was, so far as could be observed, confined to the bloodvessels of the conjunctiva, the vessels of all other mucous membranes and the skin apparently having been spared. In all probability, however, the upper gastro-intestinal tract was likewise studded with minute hemorrhages, the result of the poison upon a delicate membrane; but of this we have no proof.

CASE VIII.—*History suggestive of an acute exacerbation of a chronic nephritis; marked eosinophilia; conjunctival petechiæ; trichinosis.*

M. R., aged twenty-two years. (Service of Dr. Rudisch.) With the exception of indefinite pains in both loins and occasional urinary disturbances, the past history of this patient had been negative. Three weeks before admission the patient had complained of the symptoms of an influenzal infection; headache, fever, chilly sensations, and general body pains. The fever had subsided after a few days and had not recurred. The urine had been somewhat scanty, the face had become swollen, and the headache had continued. There had been some vomiting. At the time of the original examination the patient appeared to be suffering from nephritis, as evidenced by the puffy face and eyelids and the history of scanty urine, headache, and vomiting. The urine showed a heavy trace of albumin, but no casts. In the lower left conjunctiva were many small petechiæ. Distinct tenderness was elicited over the deltoid muscles and those of the calves. There was no fever. The blood-count was reported to be 12,600 white blood cells, of which there were 62.5 per cent. of polynuclear leukocytes, 19 per cent. of lymphocytes, and 18.5 per cent. of eosinophiles. Subsequent blood examinations revealed the presence of eosinophiles in even larger proportions, the highest count showing 37 per cent. The hemorrhages disappeared within a few days. The stools contained no ova or parasites of any kind. The diagnosis of trichiniasis was made, although the trichinæ were not demonstrated.

Petechiæ in this disease are uncommon, and so could not have been of any great assistance here in determining the diagnosis. This case is interesting, however, and illustrates the wisdom of looking for hemorrhages where trichiniasis is suspected.

Case IX.—*History of bite by rabid dog; increasing irritability, finally coma and death; skin petechiæ.*

H. S., aged nine years. (Service of Dr. Koplik.) Twenty-six days before admission this patient had been bitten on the face by a dog. The next day both patient and dog were taken to the Pasteur Institute, where the dog was killed and proved to have had rabies. The child had then undergone eighteen treatments at the institute, and had been discharged about ten days before admission to Mt. Sinai Hospital, apparently cured. Three days afterward he had suffered an attack of prolonged vomiting. Since then there had been increasing restlessness, irritability, delirium, and finally, the day before admission, coma. In addition the parents had noticed for two days a peculiar twitching of one side of the mouth for several minutes at a time. There had been no convulsions, no photophobia, no history of the refusal of water. The physical examination revealed a child in coma, absolutely unresponsive, with slight spasticity of the lower extremities, a Macewen sign, and an occasional clonic twitching of one side of the face, especially at the angle of the mouth. Over the chest, the

lower abdomen, the shoulders, and in the folds of the elbow were many small but unmistakable petechiæ. There was no neck rigidity, no Kernig, no Babinski sign, no tâche cérébrale. The temperature was 104° On lumbar puncture, 20 c.c. of faintly turbid fluid under slightly increased pressure was obtained. The bacteriology of the fluid was negative; there were no meningococci, no tubercle bacilli. Of the cells seen, 90 per cent. were lymphocytes, 10 per cent. polynuclear leukocytes. The child's condition steadily grew worse, and he died fifteen hours after admission.

In the diagnosis of this case, petechiæ were valueless. Without the previous history of a dog-bite, the diagnosis of rabies, which this in all probability was, though no necropsy was obtainable, would have been impossible, the acute onset, the previous irritability, the coma, and the petechiæ especially, indicating an epidemic cerebrospinal meningitis. This case is reported merely as another example of the occurrence in children of a hemorrhagic eruption in conditions resembling "spotted fever."

Case X.—*History and signs of acute appendicitis; chills and fever; petechiæ in conjunctivæ; weak heart sounds; diagnosis of bacterial endocarditis with mesenteric embolus; acute gangrenous appendicitis found at operation.*

D. C., aged twenty-nine years. (Service of Dr. Lilienthal.) The history had been negative, with the exception of an attack of somewhat similar nature, although not so severe about four months previous to admission. Five days before admission the patient had complained of headache, mild epigastric pain, and general weakness, had gone to bed, and had apparently improved for two days, when he had suddenly vomited and complained of severe pain in the right iliac region, accompanied by fever and chilly sensations. The last three symptoms had continued to date. There was no history of hematemesis or melena. The physical examination was extremely interesting. The patient looked acutely ill. The temperature was 102°. On account of the abdominal symptoms, the abdomen was first examined. Marked tenderness over the entire right lower quadrant, some rigidity, less tenderness over the remainder of the abdomen, and the suggestion of movable flatness pointed to the diagnosis of appendicitis. In doing the remainder of the physical examination in a routine way, four distinct petechiæ were discovered in the right and three in the left conjunctiva. The heart sounds were found to be extremely weak, but there was no evidence of an endocardial murmur. Despite this, the diagnosis of bacterial endocarditis with a mesenteric embolus was hazarded, the possibility of an acute gangrenous appendicitis, however, having been kept in mind and the surgical indication recognized. The patient was operated upon immediately and a gangrenous appendix with spreading peritonitis found. The patient made an uninterrupted recovery, and was

discharged in about two and a half weeks after his operation. The petechiæ disappeared in seventy-two hours after admission.

The etiology of the petechiæ here is a matter of conjecture. That they were manifestations of a bacteriemia secondary to a diseased appendix can hardly be considered, inasmuch as appendicitis is practically never followed by a general systemic infection, pylephlebitis and multiple liver abscesses without a bacteriemia being the usual sequelæ of a fulminating or a neglected case. Infective endocarditis may be eliminated by the disappearance of the petechiæ, the absence of a cardiac murmur, and the speedy recovery of the patient. We must be satisfied with the explanation that although the patient did not appear much prostrated, the toxemia nevertheless must have been sufficiently intense to have produced the conjunctival hemorrhages. A similar case was seen and operated upon several years ago by Dr. Elsberg, by whose kind permission I am citing the case. Here there had been a history, dating back several days, of abdominal pain and gastric distress, together with joint pains and a petechial eruption around the joints. There were petechiæ in the conjunctivæ. It was difficult to decide between a gangrenous appendicitis and "visceral crises of the erythema group." Prompt operation revealed the former condition. Here a culture of the sticky pus around the appendix was taken and reported to contain the proteus vulgaris.

Besides their importance in diagnosis, petechiæ may be considered to have some value in prognosis. In these days, when so much work is being done upon endocarditis accompanied by bacteriemia, one is prone to look with suspicion upon every case of endocarditis with petechiæ. Such a suspicion is justifiable, of course, but one must bear in mind the possibility, as evidenced by the foregoing examples, of other causes of petechiæ; so that what is most important to the patient, the prognosis, should not be definitely stated until bacteriological methods have confirmed the diagnosis. In children under ten years of age I have seen several cases of endocarditis, and one case of endopericarditis, with fever, chills, conjunctival and palatal petechiæ, which were clinically cases of bacterial endocarditis, give a negative blood culture, and so far as their acute symptoms are concerned, become entirely well. In other infectious diseases, as in typhoid fever, pneumonia, and the acute exanthemas, the presence of petechiæ renders the prognosis serious but not necessarily fatal. Where these hemorrhages are present, the case is often a fulminating one. Likewise in chronic nephritis and in other conditions of renal origin, petechiæ indicate extreme toxemia. The few cases reported will serve, I trust, to prove the value of petechiæ in diagnosis and prognosis, and to encourage the physician to hunt for them in the skin, in the mouth, and in both upper and lower conjunctivæ, in any questionable case.

THE NEUTROPHILIC BLOOD PICTURE IN PERNICIOUS ANEMIA: A PRELIMINARY REPORT.

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In the course of some work on the Arneth blood picture in various conditions, the multiplicity of lobes of the neutrophiles in a case of pernicious anemia was observed. This particular point has since been studied in nine consecutive cases seen during the past year and in the stained smears from three others. The rather striking results found, together with the lack of mention of this feature in the text-books and monographs in general use, have prompted the publication of a preliminary report in order that further observations by others may be recorded.

So far as could be ascertained in a search of the literature, the only mention of similar findings were two. v. Decastello,[1] reporting a case of splenectomy for pernicious anemia, in speaking of the blood picture, noted the abnormal number of nuclei of the neutrophiles, "abnormen Kernpolymorphismus." Brosamlen,[2] in a discussion of the blood in pernicious anemia during remissions, stated that an Arneth shift to the right was present in all cases (seven), but gave no figures. All the standard text-books dismissed the neutrophiles in pernicious anemia with the statement that they were, as a rule, diminished, both relatively and absolutely.

In the present note attention is called to the fact that in ten out of twelve cases a decided increase in the normal number of lobes of the nuclei of the neutrophiles was found, *i. e.*, a "shift to the right" in the terms of Arneth. It is further shown for comparison that in eight cases of correspondingly severe anemia, not of the idiopathic pernicious variety, seven showed either a normal number, or a decrease in the number of lobes, a "shift to the left."

There is no intention of entering here into a discussion of the value of the Arneth count. In this work it has been utilized simply as a convenient method for the study and classification of the neutrophiles. As is well known, the neutrophiles can be divided into five classes according to the number of separate lobes of their nuclei. The classical formula of Arneth was 5 per cent. in the first class, 35 per cent. in the second, 41 per cent. in the third, 17 per cent. in the fourth, and 2 per cent. in the fifth. The majority of workers have reported formulæ approximating this, it being

[1] Splenektomie bei perniziöser Anämie, Wien. med. Woch., 1913, xxvi, 951.

[2] Ueber die Bedeutung der Megalocyten bildund und über die Blutbefunde in den Remissionsstadien der perniziösen Anämie, Deutsch. Arch. f. klin. Med., 1913, cxii, 83.

found remarkably constant in normal bloods. "Shifting to the left," or an increase in the lower classes at the expense of the higher, has been regularly found in most infections and in many other pathological conditions. "Shifting to the right," the opposite of this, although noticed occasionally, has not been considered characteristic of any particular condition.

In the present series the technique used in counting has been uniform and was given in detail in a former paper.[3] Differential counts were made on the basis of 500 leukocytes and nuclear counts on the basis of 200 neutrophiles. The five chief classes of the original Arneth were adhered to with the "index" as the sum of the first, second, and one-half the third classes, a figure arbitrarily adopted as an easy means of comparison. Nuclei connected by anything more than the finest thread were counted as single. Nuclei plainly superimposed upon another were classed separately, and where doubt existed the cell was not tabulated.

The cases were from the medical service of the University of California Hospital and the private practice of Doctor Herbert C. Moffitt. Patients' histories are not given, but of the cases in Table I the diagnosis was made in each of idiopathic pernicious anemia of Biermer, both from a clinical and a hematological standpoint. In Table II the clinical diagnosis is given. For the sake of brevity descriptions of the red cells are omitted. In all the pernicious anemia cases, however, they exhibited the characteristic changes to greater or less degree, *i. e.*, increase in average diameter, high color, alterations in shape and size, and abnormal variations in staining reaction. In the other cases the diameter was normal or less than normal, central pallor was marked, and the various other pathological changes were less noticeable.

Discussing briefly the findings shown in Table I, it will be noted that Cases 1, 3, 5, 6, 7, 9, 10, 11, and 12 present distinctly abnormal neutrophilic pictures, in that at least three-fourths of the cells have three or more pieces to the nucleus. It may be remarked parenthetically that class five contains those cells having five or more lobes, and not infrequently nuclei may be seen having as many as eight separate pieces. Cases 2 and 8 show normal formulæ. The first observation on Case 4 shows a shifting to the right, but the two subsequent examinations show counts which come just within the normal range. The severity of the case has apparently no bearing on the degree of shifting, Cases 4 (at the time of the first observation), 6, and 9 being the gravest of the series. Case 7 was in excellent condition, yet showed a tremendous alteration in his picture. Seemingly against this statement is the fact that in Cases 4 and 10, as the general condition improved, the neutrophiles approached the normal, and in Cases 5, 6, and 9, as the

[3] Le Roy H. Briggs, The Clinical Value of the Arneth Method of Blood Examination, California State Jour. Med., 1912, x, 337.

TABLE I.—PERNICIOUS ANEMIA.

Case number.	Date.	Hemoglobin (Dare) per cent.	Red blood cells.	Normoblasts, per c.mm.	Leukocytes.	Neutrophiles, per cent.	Large mononuclears and transitionals, per cent.	Lymphocytes, per cent.	Eosinophiles, per cent.	Basophiles, per cent.	Myelocytes per cent.	Neutrophiles. Class I.	Class II.	Class III.	Class IV.	Class V.	Index.
Case 1, J. R. S.	April 1, 1909	38	1,609,000	Few	2,800	62.8	2.8	31.2	3.2	0	0	0	20.0	35.0	34.0	11.0	37.5
Case 2 U. C. H., No. 2752	Sept. 26, 1910	40	2,292,000	Few	4,800	71.4	4.0	21.6	3.0	0	0	2.5	27.0	43.5	22.5	5.0	51.25
Case 3, Li.	Sept. 11, 1912	45	1,968,000	0	6,000	74.0	3.8	20.6	1.2	0.4	0	2.5	16.0	42.0	28.5	11.0	39.5
Case 4	Feb. 18, 1913	10	510,000	700	2,160	56.6	6.6	36.6	0.2	0	0	2.0	13.0	40.5	34.5	10.0	35.25
U. C. H., No. 5298	April 8, 1913	45	2,372,000	0	5,000	50.0	8.0	37.4	4.6	0	0	3.5	25.0	45.5	18.0	8.0	51.25
	Oct. 15, 1913	55	2,872,000	0	7,.00	51.6	12.0	30.4	5.6	0.2	0	5.5	25.0	39.0	25.5	5.0	50.0
Case 5	April 15, 1913	45	2,228,000	0	4,060	65.6	5.6	26.8	1.6	0.4	0	0	16.0	49.5	28.0	6.5	40.75
U. C. H., No. 5550	May 5, 1913	50	2,996,000	0	4,200	57.2	8.4	30.0	4.0	0.4	0	0.5	22.5	51.0	21.0	5.0	48.5
	Dec. 20, 1913	40	2,406,000	Few	5,400	53.4	12.8	27.8	5.8	0.2	0	0	9.5	47.0	29.5	14.0	33.0
	Jan. 7, 1914	35	2,841,000	0	7,100	66.6	9.4	22.0	1.8	0.2	0	0	13.0	42.5	34.0	10.5	34.25
Case 6	April 28, 1913	15	1,078,000	400	2,800	59.0	7.0	31.6	2.4	0	0	3.0	17.5	39.5	29.0	11.0	40.25
U. C. H., No. 5582	May 5, 1913	20	969,000	1600	4,800	73.8	2.4	21.0	2.2	0.4	0.2	2.0	10.5	42.5	26.0	19.0	33.75
Case 7, Ha.	May 26, 1913	60	2,504,000	0	9,300	64.4	4.4	26.2	5.0	0	0	0	4.5	24.0	38.5	33.0	16.5
Case 8	Oct. 8, 1913	55	2,960,000	Few	8,100	61.0	12.2	24.0	2.6	0.2	0	3.5	36.5	44.0	15.0	1.0	62.0
U. C. H., No. 6279	Dec. 9, 1913	70	4,920,000	0	5,900	53.4	10.4	31.0	4.2	1.0	0	4.0	30.0	50.0	14.5	1.5	59.0
	Feb. 27, 1913	80	5,672,000	0	7,200	48.6	11.0	38.8	0.8	0.8	0	1.0	22.0	49.0	22.5	4.0	48.25
Case 9, Hf.	Dec. 4, 1913	25	955,000	500	5,100	62.6	2.6	33.0	0	0.2	1.6	6.0	17.5	35.0	25.0	16.5	41.0
	Dec. 12, 1913	20	736,000	400	7,000	72.0	1.4	25.6	0	0.2	0.8	2.0	11.0	30.5	31.0	25.5	28.25
Case 10	Dec. 19, 1913	35	2,172,000	Rare	5,100	80.6	5.8	13.4	0.2	0	0	0.5	15.0	29.0	32.0	23.5	30.0
U. C. H., No. 6598	Jan. 16, 1914	55	3,100,00	0	6,800	57.2	11.8	28.2	1.8	1.0	0	1.0	17.5	41.5	27.0	13.0	39.25
	Feb. 10, 1914	60	3,904,000	0	5,100	48.2	7.6	39.4	3.6	1.2	0	1.0	20.5	45.5	26.5	6.5	44.25
Case 11, Gn.	Jan. 3, 1914	40	1,500,000	Few	5,000	65.4	4.0	26.4	3.6	0.2	0.4	1.5	10.5	28.5	34.0	25.5	26.25
Case 12, Hu.	Feb. 27, 1914	50	2,146,000	Few	7,200	61.2	3.8	33.6	1.0	0.2	0.2	1.5	16.0	38.5	31.5	12.5	36.75

TABLE II.—SECONDARY ANEMIA.

Case number.	Diagnosis.	Date.	Hemoglobin. (Dare) per cent.	Red blood cells.	Normoblasts per c.mm.	Leukocytes.	Neutrophiles, per cent.	Large mononuclears and transitionals per cent.	Lymphocytes, per cent.	Eosinophiles, per cent.	Basophiles, per cent.	Myelocytes, per cent.	Neutrophiles.					
													Class I.	Class II.	Class III.	Class IV.	Class V.	Index.
Case 1 Pa.	Sarcoma of tongue.	Jan. 16, 1913	35	2,260,000	0	8,300	67.0	8.8	24.0	0	0.2	0	13.0	54.0	32.5	0.5	0	83.25
Case 2 U. C. H., No. 5309	Nephritis, syphilis, terminal pericarditis.	Feb. 20, 1913	15	1,800,000	0	14,400	79.6	3.6	10.8	4.6	1.4	0	3.5	37.0	43.0	15.0	1.5	62.0
		Feb. 25, 1913			Few		84.6	7.4	6.2	1.4	0.4	0	8.5	45.0	40.0	6.5	0	73.5
Case 3 U. C. H., No. 5838	Possible Banti.	June 28, 1913	50	3,120,000	0	5,100	65.8	8.8	18.4	6.6	0.4	0	18.0	57.5	22.5	2.0	0	87.25
		Sept. 24, 1913	60	3,720,000	0	6,200	58.8	7.0	16.4	16.4	1.4	0	16.0	59.0	24.5	0.5	0	87.25
Case 4 U. C. H., No. 5848	Syphilis	June 28, 1913	38	3,000,000	Rare	9,700	65.4	6.2	28.4	0	0	0	2.5	13.0	47.0	26.5	11.0	39.0
Case 5 U. C. H., No. 5828	Duodenal ulcer with hemorrhage	June 28, 1913	20	2,064,000	0	9,900	69.0	15.0	15.8	0	0.2	0	7.0	38.0	40.5	11.5	3.0	65.25
Case 6 U. C. H., No. 5944	Cirrhosis of liver with hemorrhages	July 20, 1913	18	1,516,000	Rare	14,400	73.6	4.2	21.8	0.4	0	0	2.5	35.0	41.0	18.5	3.5	58.0
Case 7 U. C. H., No. 6379	Chronic lymphatic leukemia	Oct. 24, 1913	35	2,550,000	Many	225,000	2.0	1.0	97.0	0	0	0	19.5	43.5	25.5	7.5	4.0	75.75
Case 8 U. C. H., No. 6485	Probable malignancy of intestine.	Nov. 17, 1913	10	1,800,000	0	11,900	64.2	14.3	17.9	2.7	0.4	0.3	4.5	40.5	43.0	10.5	1.0	66.5
		Dec. 10, 1913	10	2,400,000	0	11,800	72.0	9.2	13.4	4.4	1.0	0	3.0	31.0	52.5	10.5	3.0	60.25
		Jan. 15, 1914	18	2,312,000	250	14,200	75.8	10.8	10.8	2.2	0.4	0	2.5	36.5	43.5	16.0	1.5	60.75

general condition grew worse, the shifting to the right became more marked. Case 8, an early case which improved greatly, however, presented normal formulæ at two observations and a very slight shifting to the right at a third.

Table II is inserted simply for comparison as showing eight consecutive cases of approximately similar grades of anemia, not, however, of the idiopathic type. Only one of these, Case 4, shows a shifting to the right. The anemia in this case was beyond question a secondary one, but further observations were unfortunately not made. Cases 5 and 6, both anemias of rapid onset, showed normal neutrophilic pictures. Case 2 at the first examination and Case 8 throughout also showed normal formulæ, although the former died the day following the second count, and the latter was in very bad condition. The others showed a moderate degree of shifting to the left, a not unexpected finding.

Nothing further can be said in this note. Its purpose is simply to call attention to the increased number of nuclear particles of the neutrophiles in pernicious anemia, a point doubtless noticed many times before, but evidently worthy of further study.

REVIEWS

DISEASES OF THE SKIN. By GEORGE THOMAS JACKSON, M.D., Late Professor of Dermatology, College of Physicians and Surgeons, New York; Consulting Dermatologist to the New York Infirmary for Women and Children; Member of the American Dermatological Association and New York Dermatological Society, etc. Seventh edition; 770 pages; 115 illustrations; 6 plates. New York and Philadelphia: Lea and Febiger, 1914.

DR. JACKSON'S admirable, compact little volume has been thoroughly revised and a considerable number of new illustrations added. The book is alphabetically arranged so as to be a ready reference hand-book for the student and general practitioner. Thirty-two pages have been added to the last edition to bring the present work up to date. New sections have been added on acarodermatitis, cutis verticis gyrara, eczema marginatum, eczematoid dermatitis, erythema figuratum perstans, gangosa, granuloma coccidioides, ground itch, hemisporosis, keratodermia gonorrhoica, leukemia cutis, lichenification, lichen nitidus, lichen planus sclerosus et atrophicus, and trypanosomiasis. Several of the old sections have been rewritten.

The work is made of greater value by articles on vaccine treatment, written by Dr. M. F. Engman; on the administration of salvarsan, contributed by Dr. John A. Fordyce; and on Roentgen therapy, compiled by Dr. G. M. MacKee. An admirable photomicrograph of the Spirocheta pallida; a water-color painting of sporotrichosis, and several excellent practical clinical photographs have been supplied to the present volume by Drs. H. Noguchi, Howard Fox, and Arndt.

The twelve-page appendix, filled with well-known and time-honored prescriptions, is a valuable addition to the work. There is much to commend and very little to criticise in Dr. Jackson's book, which has been so successful. There has to be a certain amount of repetition in an alphabetically arranged work on dermatology. As the pages are rather small some of the photographs are not shown to their greatest advantage. A few of the illustrations are not of the excellence of the others and might be omitted.

F. C. K.

DIE UNTERSUCHUNG DER LUFTWEGE. Ein Vortrag zur Einführung in die moderne Rhino-laryngologie für Aerzte und Studierende. By DR. P. H. GERBER, A. O. Professor und Direktor der Koneglichen Universitats-Poloklinik für Hals und Nasenkranke zu Konigsberg I. Pr. Pp. 49; 61 illustrations. Wurtzburg: Verlag von Curt Kabitzsch.

IN his introduction Professor Gerber states that he has prepared this pamphlet, for in size at least, it is only that, with the help of his assistant Dr. Schlesinger, and Dr. Greene of New York, in order to broaden the knowledge of the profession in general as to the principles of the modern methods used in the examination of the upper and lower air passages. It seems to the reviewer that this idea is perfectly sound and that this little work would not be out of place in the hands of every practitioner in the least interested in the diagnosis of pathological conditions of the upper respiratory tract. Like most modern German works on the nose and throat the illustrations are excellent; and also like many of them the text is simply explanatory of the illustrations. The terse, brief descriptions do not give sufficient detail of the different technics to warrant anyone attempting, for instance, such procedures as bronchoscopy. The book is devoted entirely to technic and is a good illustration of the advances made in the last few years in the methods employed in the examination of the air passages, and which have revolutionized the whole practice of rhino-laryngology.

G. M. C.

MICROBES AND TOXINS. By Dr. ETIENNE BURNET, of the Pasteur Institute, with a preface by ELIE METCHNIKOFF, translated from the French by DR. CHARLES BROQUET and W. M. SCOTT, M.D. Pp. 316; 70 illustrations. New York and London: G. P. Putnam's Sons.

THIS admirable book presents to the medical man or biologist, indeed to the interested and intelligent layman, a complete review of the present day conception of microbiology, more particularly from the French standpoint. It is not a morphological treatise, but an analysis of the normal and pathological physiology of microscopic plants and animals. The first part is devoted to a exposition of the interdependence of the plant and animal kingdoms, with a thorough analysis of the fermentations and putrefactions necessary for continuation of life upon this planet. From this the author proceeds to a consideration of commensal and parasitic symbiosis, from which it is but a step to the discussion of microbes as disease producers. A large part of the book is

devoted to the various phases of immunity. The text ends with chapters on bacterial and chemical therapy.

The book is written in a clear, easily readable, convincing style. It is admirably translated. Prof. Metchnikoff has written the introduction tracing the history of microbiology and indicating that at his suggestion Dr. Burnet was asked to prepare the work. A glossary and index are included. H. F.

HEALTH AND LONGEVITY THROUGH RATIONAL DIET. By ARNOLD LORAND, M.D., Carlsbad. Pp. 416, Philadelphia: F. A. Davis Co.

THIS volume is intended to meet the popular demand for reliable scientific information of the subject of nutrition and diet. The general principles of nutrition are laid down clearly and impartially, without too much detail. The advantages and disadvantages of all the more important foods are discussed in the light of these principles and of the author's extensive experience and observation. The book is a readable one but the physician need not look to it for new or original points of view. It is, however, as Vaughan states in the introduction, "free from the facts which render so many of the books written on this subject for the laity harmful." C. B. F.

DISEASES OF THE EYES. By C. DEVEREUX MARSHALL, F.R.C.S., Surgeon to the Royal London (Moorfields) Ophthalmic Hospital, and Ophthalmic Surgeon to the Victoria Hospital for Children, Chelsea. Pp. 303; fully illustrated. London: University of London Press, Hodder & Stoughton and Henry Frowde.

LIKE other manuals of its kind this book gives a *resume* of the present state of ophthalmic science and practice. It is not much better nor worse than the ordinary abbreviation of which there is no lack in the domain of ophthalmology. T. B. S.

THE PSYCHOLOGY OF INSANITY. By BERNARD HART, M.D., (Lond.), Lecturer in Psychiatry, University College Hospital Medical School. Pp. 173. New York: G. P. Putnam's Sons.

IN this small volume the author discusses the history of insanity, its psychological conception, the phenomena of insanity, dissoci-

ation, etc. In other words, he attempts to present the so-called modern advances of insanity in a popular edition. For the study of insanity the book is of no value because it is hardly an introduction. For the layman it is worse than useless, for the layman could hardly appreciate what is being written. It seems therefore a pity that such an important subject as psychology of insanity should be presented in this manner. T. H. W.

FREUD'S THEORIES OF THE NEUROSES. By EDUARD HITSCHMANN, of Vienna. Authorized Translation by DR. C. R. PAYNE. Pp. 154. New York: Journal of Nervous and Mental Disease Publishing Company.

WHETHER one believes or not in any new philosophy, it is always of the utmost value to have a clear and authoritative presentation of the subject. So far in the English language we have had one textbook and numerous papers, none of which have given a clear and consecutive exposition of Freud's theories. This book, therefore, which was written by one of the ablest and sanest medical men in Vienna should be welcomed. Not only has the author the opportunity of knowing Freud's theories from Freud himself but he has practised them and in this book we have for the first time a clear presentation of Freudian doctrines presented in a readable and sane manner. T. H. W.

ANAPHYLAXIS. By CHARLES RICHET, Professor in the Faculty of Medicine, Paris. Translated by J. MURRAY BLIGH, M.D., Medical Registrar to the Liverpool Royal Infirmary. Preface by T. R. BRADSHAW, B.A., M.D., F.R.C.P., Senior Physician to the Liverpool Royal Infirmary. Pp. 266. Liverpool: The University Press, London: Constable & Co., Ltd.

THE progress of recent years in the study of anaphylaxis has been so rapid that only those in a position to follow most closely the scientific literature have been able to keep themselves in touch with the knowledge concerning this important group of phenomena. The significance of this condition, however, for general medicine is very great, not only because it may possibly explain certain otherwise obscure ailments, but also because of the increasing use of certain animal proteins for subcutaneous or intravenous injection as curative measures with the possibility of producing anaphylaxis. This book gives a clear, interesting, and very readable

account of our knowledge of anaphylaxis. It opens with a brief historical sketch including five pages in which are tersely summarized the important facts known at the present time with the names of their respective discoverers and dates of publication. Then follows a detailed discussion of the incubation period, duration and symptoms of anaphylaxis, the nature of anaphylactizing substances, passive anaphylaxis, anaphylaxis *in vitro*, the relation of anaphylaxis to precipitin formation and complement deviation, anti-anaphylaxis, the relation of anaphylaxis to general medicine and a final short chapter in which the authors' theory as to the nature and purpose of anaphylaxis is outlined. This book is a most valuable one for the large number of physicians who may wish to familiarize themselves with this important subject.

J. H. A.

THE HISTORY OF PRISON PSYCHOSES. By DRS. PAUL NITSCHE and KARL WILMANNS. Translated by FRANCIS M. BARNES, JR., M.D., and BERNARD GLUECK, M.D. Pp. 84. New York: The Journal of Nervous and Mental Disease Publishing Company.

THIS monograph is the thirteenth of the series issued by the Journal of Nervous and Mental Diseases. It is upon the important subject of prison psychoses. Of all sociological problems none are more important to the public and especially to the medical and legal professions than the study of our criminals or "near criminals." Especially is this true in the present excellent trend of the modern Juvenile Court. The present volume gives a historical review of the different viewpoints of prison psychoses so far as the German literature is concerned. It begins with an excellent introduction by William A. White.

This book should be in the hands of most medical men and all attorneys who are in the slightest way brought in contact with those who are unfortunate enough to come under the hands of the law.

T. H. W.

THE PRACTICE OF UROLOGY. By CHARLES H. CHETWOOD, M.D., LL.D., Professor of Genito-urinary Surgery, New York Polyclinic Hospital. Pp. 816; 6 colored plates and 310 text illustrations. New York: William Wood & Co.

THE author has presented in this volume the latest and best of the thought and practice of genito-urinary surgery. The book is one of the best, if not the best single volume treatise on the

subject of *urology*, that has appeared to date. The style of presentation is forceful, concise and well-systematized.

The book should prove not only interesting to the average physician, but unexcelled in value for the instruction of the undergraduate students in medicine. A noteworthy feature of the work is the heavy-faced printing of especially important statements throughout the book. Both author and publisher deserve professional congratulations for the general excellence and thoroughness of their respective parts.

Any remarks which are offered may be regarded, perhaps, in the light of difference of personal opinion, rather than a sustained opinion of the majority.

We do not believe that concensus of opinion will confirm the statement that the Treponema pallidum has not been found in the erroneously and so-called parasyphilitic diseases. Nor do we agree that the Wassermann reaction is not available until about six weeks after the first appearance of the chancre.

The chapter on "Sero-diagnosis and Sero-therapy" is commendable, but inadequate, especially that part devoted to a consideration of the gonococcus complement fixation test. Again, with respect to bacterins (vaccines), it is a mistake to advise "injections subcutaneously in gradually increasing dose at intervals of three or more days."

Photographic cystoscopy seems to be of little genuine value for the exact portrayal of intravesical appearances, and certainly there is little reason for the exhibition of Luy's separator in a work on up-to-date urology.

It is doubtful if the majority of urologists have ever observed benefit from the use of methylene blue in the treatment of gonorrhea or cystitis, or would sanction the employment of a catheter "always" in irrigating the posterior urethra in acute urethritis.

As a whole the work is very commendable, and the chapter on contracture of the neck of the bladder is a masterpiece by the man who above all others has perfected the operation most useful for its treatment.

B. A. T.

HANDBUCH DER HYGIENE. BY PROFESSORS M. V. RUBNER, M. GRUBER, and M. FISHER. Leipzig: S. Hirzel.

VOL. III, Part 3, of this Handbuch treats of the pathogenic animal parasites (protozoa, worms, and arthropods) and contains 192 illustrations in the text and 32 colored plates. The book consists of an introduction to general parasitiology by Th. von Wasielewski; a chapter on parasitic protozoa by Wasielewski; a

chapter on parasitic worms by Wasielewski and G. Wülker; and a chapter on parasitic arthropods by W. von Schuckmann.

The diseases produced by the various parasites are indicated briefly in each case. The modes of infection are given in considerable detail and the intermediary hosts of the different parasites are enumerated. The prophylactic measures are emphasized, especially the methods of campaigns against the intermediary hosts carrying the parasites.

The control of the animal parasites is a culture problem, which, unconsciously, for thousands of years has affected all civilized people. The draining of the Campagna by the ancient Etruscans protected against malaria; the prohibition of the use of raw flesh and fish protects civilized people against the danger of infection by worms; but only the knowledge of construction, life, and mode of transmission of these parasites has pointed the way to accomplish this.

The presence of the protozoa is manifested in their influence on the host by (*a*) the number of parasites present, (*b*) the place where they are localized, and (*c*) the nature of their metabolic products.

In each chapter there is a brief discussion of the history of our knowledge of the different groups of parasites, followed by a description of their form and size, construction, life-activities, nutrition, division, multiplication, acquirement of parasitic functions, movements, action on the cells of the host, modes of dissemination, the insect hosts concerned in the maturation and dissemination of the parasites.

At the end of each chapter is given a list of all the important books and papers bearing on the subject. This volume is up-to-date in every respect and is a valuable contribution of this important branch of the broad subject of hygiene. D. H. B.

SURGERY AND DISEASES OF THE MOUTH AND JAWS. By VILRAY PAPIN BLAIR, A.M., M.D., Professor of Oral Surgery in the Washington University Dental School, and Associate in Surgery in the Washington University Medical School. Pp. 638; 384 illustrations. St. Louis: C. V. Mosby Co.

WITHIN the last year or two an unusual number of new books on this subject have appeared, probably in response to the great demand on the part of medical men for a better knowledge of the mouth and jaws, and on account of a broadening of the field of the dental student. No book hitherto published so well fulfils this dual object as the volume under consideration.

The first chapter is devoted to physical examination and to anatomical considerations, followed by short chapters on general surgical pathology, discussing inflammation, tumors, hemorrhage, shock, wounds, and other injuries, for all of which information the dental student would otherwise have to consult works on general pathology and surgery. Then the various surgical conditions affecting the special parts are taken up in detail, the method of dealing with the different regions separately being followed as much as possible.

For the dental student, the book contains rather more than he requires to know of the major affectious of the face and jaws, particularly in regard to treatment. For the general surgeon especially interested in this region of the body, Dr. Blair has provided a reference work of great value. R. H. I.

HANDBOOK OF THE DISEASES OF THE EAR. By RICHARD LAKE, F.R.C.S., Surgeon to the Royal Ear Hospital, Aural Surgeon to the Seaman's Hospital, Greenwich. Fourth edition; pp. 287; 77 illustrations, including 4 colored plates. New York: William Wood & Co..

THE fourth edition of this manual has thirty-five pages more reading matter and eleven more illustrations than the last edition by the same author in the year 1910.

The book is well adapted for the use of the undergraduate and busy general practitioner, being devoid of unnecessary comments on theories and confusing references to other authors.

B. D. P.

PROBLEMS OF LIFE AND REPRODUCTION. By MARCUS HARTOG, M.A., D.Sc., F.L.S., F.R.H.S., Professor of Zoölogy in the University College, Cork. New York: Science Series, G. P. Putnam's Sons.

THE book is primarily intended for the use of the "cultured laity" but is also of interest to the practitioner who occasionally takes journeys into the field of pure science. The author writes in a popular style, is careful to define practically every term that he uses, and they are many, and lays emphasis upon every topic that may interest the general reader. In spite of this, in some of the chapters, as on cell division he plunges into the subject quite deeply, perhaps a little too much so to hold the attention of those not directly interested in the subject. However, he shows that

he has a good command of the subject and introduces much material which is engaging the attention of researches in this field at the present moment. This is particularly true of the chapter on the "new force" mitokinetism. Far more readable for the general student is the chapter on the transmission of acquired characters. The combative nature of the author is here well seen. After accusing the Weismannists of unfair attacks upon the transmissionists he makes a counter attack. If one seeks a conservative, emotionless, consideration on any subject of which he treats they will seek without success in the pages of this book. The next chapter is a criticism of Dr. G. Archdall Ried's attack as he calls it on modern Lemarckianism. From the standpoint of the general reader the chapter could have been omitted with advantage. The vitalistic view of life is later discussed and the shortcomings of the "mechanical" and "physicochemical" explanations of vital phenomena referred to. Then follows a review of the writings of Samuel Butler. The final chapter is an address to teachers on the teaching of "nature study." E. L. P.

DISEASES OF THE THROAT, NOSE, AND EAR FOR PRACTITIONERS AND STUDENTS. By W. G. PORTER, M.B., B.Sc., F.R.C.S. Ed., Surgeon to the Eye, Ear, and Throat Infirmary, Edinburgh; Surgeon, Ear and Throat Depart., Royal Hospital for Sick Children, Edinburgh; Aurist to the Edinburgh Royal Institution for the Education of the Deaf and Dumb. Pp. 275; 77 illustrations, 44 in colors. New York: William Wood & Co.

THE author in writing this book has endeavored to provide, in a small volume, the practitioner and students with sufficient information on diseases of the nose, throat, and ear, so that they may have a basic knowledge of diseases of these organs as they appear in general practice and to be able to treat the simpler ones. The book is divided into four sections, one on disease of the pharynx, one on diseases of the larynx, one on the nose, and one on diseases on the ear. It is well arranged and clear and the different diseases are considered in what might be termed their natural sequence.

On the whole the book is well written and easily readable; it is up to date, and, though individual exceptions can be taken to some of the author's statements, it is a safe and reliable guide for those for whom the book was intended, namely, the general practitioner and student.

In the appendix there is a formula containing many useful prescriptions and the index is sufficiently detailed to make it a useful addition to the book. G. B. W.

THE COMING OF EVOLUTION. By JOHN W. JUDD, LL.D., F.R.S., formerly Professor of Geology and Dean of the Royal College of Science. THE INDIVIDUAL IN THE ANIMAL KINGDOM. By JULIAN S. HUXLEY, B.A., Research Associate of the Rice Institute. HEREDITY IN THE LIGHT OF RECENT RESEARCH. By L. DONCASTER, M.A., Fellow of King's College. THE PSYCHOLOGY OF INSANITY. By BERNARD HART, M.D., Lecturer on Psychiatry, University College Hospital Medical School. BREWING. By A. CHESTON CHAPMAN, President of the Institute of Brewing. Cambridge: University Press. New York: G. P. Putnam's Sons.

THESE small volumes of some 150 pages each, represent the recent additions to the Cambridge Manual of Science and Literature. The several authors are authorities in their respective fields and present their subject matter in an entertaining and lucid manner, so that the text can be followed with ease by those unacquainted with the abstruse problems of the various subjects.

These little books, while not actually pertaining to medical subjects could be read with profit by physicians interested in phases of other sciences which have a close bearing upon and intimate correlation with, the science of medicine. J. H. M., JR.

PUBLIC HEALTH CHEMISTRY AND BACTERIOLOGY. A HANDBOOK FOR DEPARTMENT OF PUBLIC HEALTH STUDENTS. By DAVID MCKAIL, M.D., D.P.H., F.R., F.P.S.G., Lecturer on Public Health and Forensic Medicine, St. Mary's College, Glasgow; Examiner in Public Health for the Department of Public Health, Scottish Conjoint Board, etc. Pp. 409. New York: William Wood & Co.

THE author presents in this volume a handbook for teacher and student from material he uses in his public health course. It is almost entirely devoted to technical examinations and makes an excellent complement to a book on theoretical and practical hygiene. The first part of the book is devoted to chemical and physical analysis of water, air, soils, food beverages, and disinfectants. The chapter on foods is especially good. The latter two-thirds are devoted to public health bacteriology. Greatest attention is paid to methods of detection and determination. At the end of the book the author devotes a chapter to special examinations of water, air, soil, sewage, and food, and winds up by giving the regulation for the diploma in public health, and a review of Parke's work on bovine and human tuberculosis. As a handbook for the sanatarian it is useful chiefly in the labora-

tory, but there are a few methods given for rapid testing in the field. It will be probably most useful to those giving courses on the subject. No illustrations are given because the apparatus is seen during instruction, the author says in the preface. H. F.

STUDIES IN CANCER AND ALLIED SUBJECTS. From the Departments of Zoölogy, Surgery, Clinical Pathology and Biological Chemistry. Conducted under the George Crocker Special Research Fund at Columbia University. Volume III, pp. 295. New York: Columbia University Press.

THIS book is a series of reprints of various articles by the numerous workers under the Crocker Fund. The reprints are arranged according to departments and preceded in two instances by interesting scientific reports of the departments by their respective heads. It is extremely convenient to have under one cover the diverse but valuable papers contained in this volume.

H. T. K.

AIDS TO DISEASES OF CHILDREN. By JOHN M. CAW, M.D., R.U.I., L.R.C.P. (Edin.), Senior Physician to the Belfast Hospital for Sick Children, etc. Fourth edition; pp. 423. New York: William Wood & Company.

BY using very thin paper and small type, the author has managed to put a surprising amount of material between the covers of an apparently small volume. Etiology, pathology, symptomatology and treatment are very fully covered as well as the anatomy and physiology of infancy and childhood. S. J. R.

ACUTE ABDOMINAL DISEASES, INCLUDING ABDOMINAL INJURIES AND THE COMPLICATIONS OF EXTERNAL HERNIA. By JOSEPH E. ADAMS, M.B., M.S. (Lond.) F.R.C.S. (Eng.), Senior Assist. Surgeon, East London Hospital for Children; Hunterian Professor, Royal College of Surgeons of England, etc., and MAURICE A. CASSIDY, M.A., M.D., B.C. (Cantab.), F.R.C.P. (Lond.), Physician with charge of Out-Patients, St. Thomas' Hospital. Pp. 571. New York: William Wood & Co.

THIS book is based on the experience of the authors as Resident Assistant Surgeon and Resident Assistant Physician respectively

to St. Thomas' Hospital. Its object is "to discuss, compare, and contrast all the various acute diseases and injuries to which the abdomen and its contents are liable, treating these conditions from the point of view of both physician and surgeon." The field is comparatively untilled, the authors' experience is large, and while we may not always agree with their interpretation of "acute," and their method of discussion involves a certain amount of repitition, the result is a most interesting and in many respects, satisfying production. To the hospital surgeon as well as to the general practitioner, it affords much information and food for thought.

E. B. H.

STUDIES IN CANCER AND ALLIED SUBJECTS. THE STUDY OF EXPERIMENTAL CANCER; A REVIEW. By WILLIAM H. WOGLOM, M.D., Assistant Professor, Columbia University, Assigned to Cancer Research. Conducted under the George Crocker Special Research Fund at Columbia University. Volume I; pp. 274; 55 illustrations and numerous charts. New York: Columbia University Press.

THE book is an octavo volume which could easily be bound in smaller compass, a volume occupying more library room than its contents require. As is indicated in the title, the work is a review and places before the reader in condensed form the material on experimental cancer which had been contributed before its appearance. Written in true scientific spirit, well illustrated, clearly printed and with ample references to the literature of the subject, the book commends itself highly to those who wish a brief but comprehensive review of this prolific and prodigous field. H. T. K.

A HANDBOOK OF SURGERY INTENDED FOR DENTAL AND JUNIOR MEDICAL STUDENTS. By ARTHUR S. UNDERWOOD, M.R.C.S., L.D.S. (Eng.), late Examiner Royal College of Surgeons of England, etc., and BAYFORD UNDERWOOD, M.B., B.S. (Lond.), L.R.C.P., M.R.C.S. (Eng.). Pp. 244; 19 illustrations. New York: William Wood & Co.

THIS little volume gives an outline of the general principles of surgery, with special reference to the parts of importance to the dental student. For his instruction also diseases of the eye, nose, and accessory sinuses, larynx, and skin are briefly described. The book should be useful to students preparing for examinations.

R. H. I.

EXAMINATION OF THE NERVOUS SYSTEM. JULIAN LOUDON, B.A., M.B., Assistant in Clinical Medicine, University of Toronto. Pp. 30. Toronto: G. A. Merrick Printing Company.

IT is simply an outline for the student so that a complete examination of the nervous system can be made. It is a question whether this is worth while after all, for if one were to follow out rigidly the scheme in its entirety, it would take about a week to examine a patient. T. H. W.

THE DOCTOR IN COURT. By EDWIN VALENTINE MITCHELL, LL.B., of the Massachusetts Bar. Pp. 152. New York: Rebman Company.

THIS work is not intended to be a treatise on Medical Jurisprudence but rather attempts to outline the relationship which the law bears to the physician on the witness stand, whether he be testifying in his own behalf or as an expert. It presents in a clear and convincing way a knowledge of the physician's duties and legal obligations which may grow out of his relations with his patients. S. J. R.

THE TREATMENT OF INFANTILE PARALYSIS. By OSCAR VALPIUS, M.D., Professor Extraordinary at the University of Heidelberg. Translated by ALAN H. TODD, M.B., B.S., B.Sc. (Lond.), House Surgeon, Guy's Hospital. With introduction by J. JACKSON CLARKE, M.D. (Lond.), F.R.C.S. New York: William Wood & Co.

VALPIUS has collected in his single volume, valuable facts which are essential in the treatment of infantile paralysis. These facts are drawn from his and many other orthopedic surgeons' experiences in the treatment of the sequelæ of this type of paralysis. He presents this subject in an attractive manner weaving into the subject his personality and his own experiences in such a manner as to impress one of his profound sincerity. It is rarely possible to translate a theme from one language to another without losing something of the author's force or shades of meaning. In the statement of facts, however, it can be done more concisely. This book in point of view of order is unchanged and probably has lost nothing of the original continuity of thought.

This work has, however, the following excellent features: The facts are grouped under headings, which arrangement facilitates reference. The treatment of the various stages and sequelæ

many and too extensive procedures among those recommended as suitable for performance in the office, and that he has so far overrated the skill of the average practitioner that he has risked placing his readers in the unenviable position of attempting operations they would be unable to carry to successful terminations. This is especially true in regard to the treatment recommended for internal hemorrhoids.

Throughout the book the author insists upon the necessity of making a thorough proctologic examination of the patient, and it is to this frequently repeated advice that much of the value of the book is due.

The book is well printed, and the illustrations are excellent. With the warning given above it may be recommended to the general practitioner as a guide in the treatment of rectal diseases.

S. W. M.

THE FITNESS OF THE ENVIRONMENT. By LAWRENCE J. HENDERSON, Assistant Professor of Biological Chemistry in Harvard University. Pp. 317. New York: The Macmillan Co.

As the title indicates, the author's object is to describe some of the natural phenomena, which are of importance to the life of organisms upon the earth. Those phenomena which he selects for special description are not the grosser aspects of Nature, however, but chemico-physical processes, and concern principally the properties of carbon, hydrogen and oxygen, and their compounds, especially water and carbonic acid. One hears much of the fitness of the organism to the environment, and of the adaptations of different parts of the organism to carry out certain functions. Here is presented the other side of the relationship: the characteristics of some of the elements and compounds which are of fundamental importance in making the environment suitable for the physiological processes of living plants and animals. The conclusion is that Darwinian fitness is a perfectly reciprocal relationship: a fit organism inhabits a fit environment. W. H. F. A.

SYSTEMATIC CASE-TAKING. By HENRY LAWRENCE MCKISACK, Physician to the Royal Victoria Hospital, Belfast. Pp. 166; 1 illustration, New York: Paul B. Hoeber.

THE term "case-taking" must not be confused with history-taking, for the author uses it to embrace the acquiring of all information, both subjective and objective, necessary to make a

diagnosis. The amount of space devoted to the sub-head, pain and to the chapter on the nervous system, seems unnecessarily full, but possibly these subjects have received too scanty consideration heretofore. The work serves to emphasize the too oft neglected fact that only by systematic case-taking can a trustworthy diagnosis be reached. S. J. R.

LECTURES ON DISEASES OF CHILDREN. By ROBERT HUTCHINSON, M.D., F.R.C.P., Physician to the London Hospital and Physician to Hospital for Sick Children, Great Ormond Street. Third edition. Pp. 404; 69 illustrations and 13 diagrams. New York and London: Longmans, Green & Co., and Edward Arnold.

THE book embodies a series of lectures first given in the London Hospital in 1902, with subsequent revisions, and covers the most important diseases found in infants and children exclusive of the exanthemas and the acute contagious diseases such as diphtheria, pertussis, etc. It is essentially a clinical presentation clearly based upon careful, painstaking and extensive observation, and contains many valuable suggestions, and descriptions not found in the average text-book. Because, however, of the limitation of the number of subjects considered, it cannot be considered in any sense as a text-book upon pediatrics. As very delightful and instructive collateral reading, however, it well deserves a place upon the pediatric book-shelf. J. C. G.

THE HEALTHY BABY. By ROGER H. DENNETT, M.D., Instructor in Diseses of Children in the New York Post-Graduate Medical School, etc. Pp. 235. New York: The Macmillan Company.

THE book is intended to make clear to the mother the best way to do the every-day things that have to be done for a child, and the author should take satisfaction in having performed his task well. The book is divided into six parts, dealing with development and the bodily functions, hygiene and training, common ailments, care of the special organs, feeding and diet, lists and tables. No attempt is made anywhere to usurp the office of the family doctor or to become the "universal pediatrist." It is a collection of good advice in plain non-technical language, and aims at prevention rather than cure. Feeding and diet is such a large and unsettled subject that it does not pay to be too didactic. This is the only part of the book to which exception might be taken. While a large number of pediatrists will agree

with the sentiments here expressed, there is likely to be a considerable group who would differ with these ideas. The manner of modifying the milk would probably be the chief bone of contention, but there are several minor points which would give ground for difference of opinion. In spite of these objections the work is of value, and the physician who recommends it to his patients will probably earn their gratitude. S. J. R.

SCHOOL HYGIENE. By FLETCHER B. CRESSLER, PH.D., Specialist in School Hygiene and School Sanitation, U. S. Bureau of Education. Pp. 369; 51 illustrations. New York: The Macmillan Company.

IN outlining the purpose of his book the author states that it is not written for the specialist in school hygiene but for the busy teacher. Indeed, the final goal of the author's effort seems to be the hardened and custom ridden mind of school boards, reached through intelligent insistence on the part of well informed teachers. The selection of topics is based on their practical importance and all are treated in a most painstaking way. A. A. H.

TREATMENT OF INTERNAL DISEASES. By PROF. NORBERT ORTNER, of the University of Vienna. Edited by NATHANIEL BOWDITCH POTTER, M.D., Assistant Professor of Clinical Medicine at Columbia University, New York. Translated by FREDERIC H. BARTLETT, M.D., Instructor of Children's Diseases at Columbia University. From the fifth German edition; pp. 640. Philadelphia: J. B. Lippincott Company.

THE second American edition of this therapeutics is translated from the fifth German edition. It follows closely the plan of the previous edition and on the whole has undergone but few changes. Professor Fronz, of Vienna, has entirely rewritten the section on children's diseases, while here and there throughout the text occasional minor changes and additions have been made. The editor has wisely omitted such drugs as are not sanctioned by the Council of Pharmacy and Chemistry of the American Medical Association, but he has retained many which are inactive and totally unknown. A change that would have greatly improved the book would have been to abbreviate the number of prescriptions and at the same time reduce the number of drugs that are found in so many of the formulæ.

Another criticism that might be made is that nothing is said of some of the newer methods of treatment that have come into use since the last edition. For example, nothing is said of the treatment of leukemia with benzol, of the removal of the spleen for pernicious anemia, of vaccine therapy, or fresh air in the treatment of croupous pneumonia, and of many other advances in modern therapy. Even if the author or the editor does not approve of nor advocate such methods, yet would it not be of advantage to the reader to know his experience with these procedures and to know why he does not approve of them? Disregarding these comparatively few criticisms and omissions the book is a splendid compilation of practical treatment—of treatment in all its forms, whether dietetic, hygienic, physical, mechanical, climatic, or medicinal.

J. H. M., Jr.

THE NEW PUBLIC HEALTH. By H. W. HILL, M.B., M.D., D.P.H., Director Institute of Public Health, London, Ontario. Pp. 128. Minneapolis: Press of the *Journal-Lancet*.

IN this book are collected a series of monthly articles on Public Health Topics, which originally appeared in the *Journal-Lancet*, of Minneapolis. It is meant for general reading and especially recommends itself for this purpose by its conciseness, clearness, and the logical way in which the essential factors which comprise the great public health problem are treated.

The author feels that the public or primary routes of spread of disease are thoroughly understood. He therefore lays special stress on the secondary or contact sources of spread. It is in this latter direction that he declares future progress will be made.

The crux of the situation to him is the individual, the fountain head of contagion. He holds universal enlightenment above coercion and outlines a means for its accomplishment.

A. A. H.

DISEASE AND ITS CAUSES. By W. T. COUNCILMAN, A.M., M.D., LL.D., Professor of Pathology in Harvard University. Pp. 254; 19 illustrations. New York: Henry Holt & Co., 1914.

THIS latest addition to the HOME UNIVERSITY LIBRARY is a valuable one, and is of special interest to the medical profession, not in that it contains any new or special information, but in that it puts in the hands of the layman the kind of knowledge he should have for the proper forming of his conceptions of disease as it occurs in his daily experience.

Such simple and clear presentation of basic medical truths is bound to bear its fruit in hastening the advent of a state of general enlightenment.

The author's discussion of disease in its general aspects is good. His more more specific teachings as regards the bacteria, infections, carriers, immunity, chronic disorders, heredity, and eugenics are to the point.

The aim of the book is clear, and is well expressed in the author's words, "No measures of preventive medicine are successful which are not supported by a public educated to appreciate their importance." A. A. H.

A Manual of Operative Surgery, with Surgical Anatomy and Surface Markings. By Duncan C. L. Fitzwilliams, Lecturer on Clinical Surgery and Joint Lecturer on Operative Surgery, St. Mary's Hospital Medical School. Pp. 446; 284 illustrations. New York: William Wood & Company, 1914.

This is a text-book for the "apprentice" and "journeyman craftsman of our profession," and is not intended for a "master of the art" of surgery. With this main purpose of the author in mind the reader will find it a well-constructed book of a useful kind. It will be most useful to the undergraduate student, but the surgeon, particularly the younger surgeon, will find it serviceable. It has the compactness to be expected from the author's long service in preparing for examinations. There are few references, quotations, or repetitions, but there is the marked preference for English operations that one would look for from an English author. There is no reference to the Larrey amputation of the shoulder, a brief reference to Wyeth's pins, but no mention of the method of amputation of the hip necessary to make them serviceable. The references to surgical anatomy are appropriate, the discussion of strangulated hernia particularly good, of necessity, less formal than of most operations, but very practical. There is need of a similar discussion of the conservative surgery of the hand and the relative value of the various amputations of the foot. On the whole the book fulfils well the purpose for which it was intended. T. T. T.

Maternity Primer. By A. H. F. Barbour, M.D., LL.D., Physician to the Edinburgh Maternity Hospital. Pp. 165; 67 illustrations. New York: William Wood & Co.

This book is a set of notes for the use of nurses commencing their maternity training. Pregnancy, labor, and the puerperium

are pictured as a normal sequence. Placenta prævia receives especial attention, and the responsibility as well as the limitations of the nurse in such cases are emphasized. The proper treatments in this and other emergencies are clearly given. Sepsis is also closely studied, and is presented as a preventable condition.

A. A. H.

ARTIFICIAL PARTHENOGENESIS AND FERTILIZATION. By JACQUES LOEB, of the Rockefeller Institute for Medical Research. Translated from the German by W. O. R. KING and supplemented and revised by the author. Pp. 322; 87 illustrations. Chicago: University of Chicago Press.

IN this work of Dr. Loeb's is found a *resumé* of his well-known results upon artificial parthenogenesis together with some new material not hitherto published. Through chemical and physical agencies he endeavors to produce the effects of the sperm upon the egg and by this means to arrive at an understanding of that phase of fertilization concerned in inaugurating development. He comes to the conclusion that the formation of a membrane by the egg is the primary cause of its development, and that there is then necessary some agent to stop this process from continuing too far. Membrane formation may be accomplished by the action of any cytolysing agent. The cytolysis must be stopped when only the surface of the egg is involved, and this is accomplished through the action of hypertonic sea water. Accelerated oxydation follows the superficial cytolysis and this results in cell division. As an explanation of such action Loeb offers the suggestion that the surface of the egg is an emulsion, and that cytolytic agents destroy its stability. Eggs vary in the degree of this stability and some easily exhibit artificial parthenogenesis. Regarding normal fertilization the conclusion is that the sperm, aside from its action in heredity, has the double function of bringing into the egg a cytolysing agent to start membrane formation and a second to stop the action of the first when this has been accomplished. There are 32 chapters in the book and a general analysis of artificial parthenogenesis and related subjects in various animals is given.

Mc. C.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Successful Cultivation of Leishmania Donovani from the Blood.—M. MAYER and H. WERNER (*Deutsch. med. Woch.*, 1914, xl, 67) have had under observation a patient suffering with tropical splenomegaly (kala-azar). Diagnosis was made by the finding of Leishmania donovani in the material obtained by splenic puncture; the organisms were cultivated from this material on Nicolle's modification of the Novy-MacNeal medium. The discovery of the parasites in the peripheral blood is usually possible only in the late stages of the disease; in the early stages it is only after prolonged search, and then only exceptionally, that the organisms are found. The authors inoculated a dozen tubes of media with the patient's blood, adding three to five drops to each tube. The tubes were examined every eight days, and after one month five tubes showed a growth of Leishmania donovani. The demonstration of viable parasites in the peripheral circulation is of considerable importance because of the possibility of the transfer of infection by blood-sucking insects. Novy has succeeded in cultivating the organisms from the blood of experimentally infected dogs, but the authors have been unable to find a report of a successful culture from human cases.

Hypercholesterinemia and its Role in the Production of Gall-stones.—According to CHAUFFARD and his pupil, Grigaut (*Presse. Méd.*, xxi, 929 to 932), whose method was used in the cholesterin determinations, there occurs a true hypercholsterinemia in cases of jaundice, gall-stones, typhoid fever, and pregnancy. In typhoid fever this develops after the febrile period and becomes maximum at about

the seventh month of pregnancy. The cause in these conditions is to be found in a hyperactivity of the adrenals, and perhaps in the corpus luteum as well. It is clearly recognized that typhoid and pregnancy are potent predisposing causes of gall-stones, an essential condition for the formation of which is an excessive blood content in cholesterin. The author calls attention to the exogenous or dietetic origin of cholesterin, since this has some therapeutic importance, and the endogenous, arising mainly from the adrenal glands. A normal function of the liver is to rid the blood of a certain amount of cholesterin, this being excreted in the bile through the specific activity of highly specialized hepatic cells, which may further convert some of it into solvents for cholesterin itself, namely the biliary acids. When these cells fail in their normal functioning, as in cholelithiasis, one finds the adrenals unusually deficient in cholesterin, while the blood contains an increased amount and the bile is deficient in its acid content. Since all these things are evidences of one and the same thing—hepatic insufficiency—one may attribute the formation of gall-stones to a specific disturbance of certain liver cells.

Experimental Production of Pernicious Anemia.—ADLER (*Jour. of Med. Research*, xxviii, 199 to 226), having determined that the severe anemia caused by infections with Dibothriocephalus latus is due to the presence of an insoluble fatty acid capable of producing hemolysis, has been able to produce the blood picture of pernicious anemia by feeding dogs large doses of insoluble fatty acids, such as olive oil. The organism normally possesses a defensive mechanism against such acids in the shape of lymph glands, according to the author. As the result of experiments the author concludes that fatty acids are toxic directly in proportion to their insolubility. Animals given non-toxic doses over a long period of time showed some typical blood crises such as are seen in pernicious anemia. The simulataneous administration of suitable amounts of quinine protects the animals from the poisonous effects of the fats. The anemia induced is essentially due to the destructive action upon the circulating red-blood cells, for in the early stages at least the bone-marrow appears to be stimulated so that high red counts may occur. The opinion is advanced that the hemolytic substance occurs in the form of colloidal particles the effects of which depend probably upon the relation of their number to that of the red-blood corpuscles.

A Contribution to the Study of Cancer.—E. WEISS (*Deutsch. med. Woch.*, 1914, xl, 66), alludes to the possibilities of the Abderhalden test as applied to the diagnosis of cancer. The author has made interesting observations which bear on the diagnosis of gastric cancer. He finds that normal individuals, after the parenteral administration of anatomically normal gastric mucosa, develops ferments in the blood serum specific for this tissue. Repeating the experiments with the sera from two patients suffering with cancer of the stomach, he found that there was a failure to develop these ferments. If the observations prove correct when repeated with a large number of cases, he believes it may be possible to apply the method as an exact differential diagnostic aid.

Renal Diabetes.—H. SALOMON (*Deutsch. med. Woch.*, 1914, xl, 217) prefers the name diabetes innocens for the symptom-complex usually designated renal diabetes. Numerous cases have come under the author's observation in von Noorden's clinic. He finds that the condition can remain quite stationary for as long as ten years; that it often runs in families; that it is a comparatively common disease; and that a minority of the cases may exhibit an increase in the blood sugar. The clinical picture of the disease, as the author has observed it, is briefly as follows: There is a harmless glycosuria, often appearing on brothers and sisters. The onset is usually in childhood, even in infancy. A well-marked nervous temperament may be noted in those affected with the disease. The sugar in the urine is usually below 1 per cent., though occasionally for a day or in a single specimen the percentage may be considerably higher. Often mental excitement may cause an increase. The condition suggests the inability of the kidney to secrete a concentrated urine, as in diabetes insipidus. As a rule the low percentage of sugar distinguishes the condition from juvenile diabetes mellitus. Generally the total excretion of sugar with the patient on a mixed diet does not exceed 12 gm. daily. The sugar excretion is only slightly affected by putting the patient on a starch-free diet. Administration of 100 gm. glucose on a fasting stomach is followed by the excretion of not more than 10 per cent. of this amount, usually only 1 to 7 per cent. At the same time the blood sugar rises by 1 to 3 cg. (0.01 to 0.03 per cent.), though a greater increase does not invalidate the diagnosis. Ordinarily the blood sugar is present in normal amount with renal diabetes, though there may be a hyperglycemia. There is no tendency of the disease to progress. In some patients there may be a marked acetonuria on a starch-free diet; this rapidly vanishes when starch is added. Except for the nervous manifestations the patients appear to be normal individuals, and are not more subject than the normal to the usual complications of diabetes mellitus (furunculosis, neuritis, etc.). This seems to hold good also for diabetes innocens with hyperglycemia. Salomon recommends a diet for these patients containing carbohydrate equivalent to 100 to 200 gm. white bread, but after the condition has persisted unchanged for several years a more liberal diet may be allowed.

Further Observations on the Chemotherapy of Experimental Trypanosome Infections.—W. KOLLE, O. HARTOCH, and W. SCHURMANN (*Deutsch. med. Woch.*, 1914, xl, 212) have continued their observations on the treatment of experimental trypanosome infections with antimony preparations. As in their earlier work, they have continued to obtain very good results with antimony trioxide, which they designate "trixidin." Their studies show that: (1) Therapia sterilisans by means of trixidin can be accomplished in the case of chronic trypanosome infections of large animals. (2) In cases in which abscess formation has followed the intramuscular injection of trixidin, they have resorted to intravenous administration of antimony trioxide in physiological salt solution with success (rabbits, guinea-pigs). (3) A permanent sterilization of dogs suffering with chronic dourine infection may be accomplished by means of inunctions with antimony preparations. The most potent of these is apparently dimethylphenylpyrazolon-

antimony trichloride in the form of a salve. (4) The principles of treatment developed by the authors, *i. e.*, inunction, or intramuscular injection of water-insoluble (depot-forming) antimony preparations, are applicable to human cases, though it must be remembered that subcutaneous or intramuscular administration is likely to lead to abscess formation. (5) Antimony trioxide may be employed in colloidal-like solution intravenously, at least in small animals. In this form it is very active therapeutically. (6) The authors hope to determine whether the colloidal-like solution of antimony trioxide can be used in the treatment of sleeping sickness of man, possibly as an adjuvant to inunctions.

Loss of the Hypophysis, with Fatal Issue.—M. Simmonds (*Deutsch. med. Woch.*, 1914, xl, 322) reports a case with autopsy findings. The patient was a woman, aged forty-six years, who became ill with severe puerperal sepsis. There was a septic necrosis of the hypophysis, the author believes. As a result of the injury to this important organ the following symptoms made their appearance: menopause, muscular weakness, vertigo, attacks of loss of consciousness, anemia, rapid aging; in short, "senium precox." The part of the gland which remained intact doubtless gradually atrophied in the connective tissue surrounding it. The organ became absolutely insufficient and the patient died in coma. At autopsy the only adequate cause of death to be found was an almost total loss of the hypophysis.

The Blood in Hemophilia.—Howell (*Arch. Int. Med.*, 1914, xiii, p. 76 to 95). After describing in considerable detail the methods used in the preparation and estimation of antithrombin and prothrombin, Howell gives his observations made upon undoubted cases of hemophilia, studied over a period of two years. The coagulation time was determined by aspirating 2 or 4 c.c. of blood from a vein, and expelling it at once into carefully cleaned test-tubes: by this method the normal coagulation time varies between twenty and forty minutes, the end point being that time at which it was possible to invert the tube. Hemophilic blood coagulates in from two and one-half to five hours, provided the needle of the syringe enters the lumen of the vein on the first puncture. This great retardation of the normal process Howell believes is due to a true reduction in the amount of prothrombin, as a result of which the antithrombin content is relatively greater in hemophilic blood than in the normal specimen with which it is controlled. This peculiarity of the blood can be readily tested for clinically by first oxalating the blood, which is then centrifugalized to secure a clear plasma. If on adding to this plasma a suitable amount of calcium chloride, coagulation is delayed beyond nine to twelve minutes, one may reasonably suspect the existence of a hemophilic condition of that particular blood. Howell presents clearly his arguments against the numerous theories advanced by Morawitz, Wright, Wolf-Sahle, and others, which attempt to attribute the delayed coagulation time to deficiencies in thrombokinase, calcium, thrombozym, etc., and concludes by defining hemophilia as "a condition limited to the male in which the coagulation time is markedly prolonged in consequence of a deficiency in the amount of contained prothrombin, with the additional

characteristic that the defect is transmissible by heredity in accordance with the so-called law of Nasse." Though the ultimate cause is not certain the most likely one is that there exists some functional change in the blood platelets, since these appear to be the source of prothrombin. In studies upon thrombosis, Howell finds here the evidences of diminution in the antithrombin content of the plasma, prothrombin being normal, while in the so-called hemorrhagic conditions both of these constituents show no variations from the normal.

The Surgical Treatment (Splenectomy) of Diseases of the Blood.—R. Mühsam (*Deutsch. med. Woch.*, 1914, xl, 377) has had considerable experience with splenectomy in diseases of the blood. He reviews his own cases, together with those reported in the literature. He finds that: (1) Splenectomy is indicated in infectious diseases, such as typhoid and sepsis, only in case of spontaneous rupture of the spleen. (2) In malaria splenectomy has no effect on the disease. It is indicated here only where there is danger of twisting, in the case of wandering spleen, or in the rare instances where rupture occurs. (3) In leukemia extirpation of the spleen is contra-indicated. (4) In Banti's disease splenectomy if performed at the right time may result in a cure. Even in the third stage, splenectomy combined with a Talma operation may bring about a cure. (5) Severe cases of anemia splenica infantum may be saved by splenectomy. (6) In hemolytic icterus extirpation of the spleen seems to have had a very beneficial effect in a number of cases. (7) A considerable number of cases of pernicious anemia have been improved by splenectomy. In other instances the operation seems to have had no effect. The indications for operation are as yet uncertain. Caution should be exercised if there is any tendency to bleed.

The Diagnosis of Uremia by Means of Indican Determinations in the Blood-serum, Exudates, and Transudates.—G. Dorner (*Deutsch. Archiv f. klin. Med.*, 1914, cxiii, 342) has studied the indican of the blood and other body fluids in nephritics with uremic symptoms and in other patients with convulsions, following the suggestion of Obermeyer and Popper, who believed they had established the fact that a marked increase of the pigment in the blood is practically diagnostic of uremia. The technique was as follows: 10 to 20 c.c. of blood obtained by venesection or syringe were precipitated with five times the volume of 95 per cent. alcohol and filtered. The filtrate was evaporated and the residue taken up in water. This was precipitated by the addition of two to three drops of lead acetate solution, filtered and made up to 10 c.c. by the addition of water. A like amount of Obermeyer's solution was then added. The mixture was shaken in a water-bath with 1 c.c. of chloroform. A more or less intense blue color in the chloroform indicates a positive test. Dorner studied 26 patients; 7 of these had well-marked uremic symptoms and 2 suspected uremia. His conclusions were: (1) The presence of indican in the blood in large quantity is characteristic of outspoken uremia. (2) When indican is present in the blood in considerable amount it is also found in pleural exudate and anasarca fluid, but not in the spinal fluid. (3) No toxic effect can be attributed to the indican in uremia. (4) In uremia due

to lack of kidney tissue (cystic kidney autopsy) indicanemia may be absent. (5) With marked indicanuria without disease of the kidneys, indican is not found in the blood-serum in large amount. (6) It is not certain that the urinary indican is formed in the liver. It is quite possible, Dorner believes, that the kidneys are concerned in its formation. (7) The appearance of indican in the blood or transudates is a sign of approaching exitus, as a rule. However, patients with a small amount of indican in the body fluids may improve.

On the Use of Salvarsan-copper.—G. BAERMANN (*Münch. med. Woch.*, 1914, lxi, 1) reports his results in treating 45 patients suffering with amebic dysentery, frambesia, and malaria with Ehrlich's new compound, which for brevity's sake is called K_3. The number of cases treated is small and permits of no definite conclusions, but the results seem to show that the compound is a very active one. The drug may be given in 0.1 gm. dose on each of three successive days, or 0.15 gm. on two days. The latter is the maximal dose. Baermann found that the drug was entirely useless in the treatment of amebic dysentery. In frambesia it is markedly spirocheticidal. Baermann's impression is that it is more active in this disease than salvarsan. In 1 case of quartan malaria with schizonts and free gametes the parasites disappeared from the blood. In 4 cases of tertian fever with schizonts and gametes no parasites had been found two months after treatment. In 2 cases of pernicious malaria, with rings but no gametes, cure resulted (no parasites after two months). In cases of pernicious malaria with crescents the latter were unaffected, though the schizonts were destroyed. In 1 case of leprosy there was apparent improvement following the treatment. Baermann plans to continue his study and considers the results with frambesia and malaria very encouraging.

A Standard Antigen for the Wassermann Reaction.—C. W. FIELD (*Arch. Int. Med.*, 1914, xiii, 790). The antigen herewith described has been subjected to exhaustive study at the Bellevue Hospital during the past six months, and has been tried over a series of 5000 cases. The antigen consists of an alcoholic extract of guinea-pigs' hearts, half saturated with cholesterin. It is prepared as follows: 300 grams of guinea-pigs' hearts are extracted with 3 liters of absolute alcohol at 37° C. for two weeks. To one-half of the filtrate cholesterin is then added in excess and after having stayed in the incubator over night the solution is exposed to a constant temperature of 16° C. for three hours in order to throw down the excess of cholesterin. The solution is now filtered and is then added to an equal volume of the original alcoholic extract; 20 c.c. of this mixture are then evaporated to dryness at 56° C., desiccated over sulphuric acid for twenty-four hours, and then weighed. In this way is determined just what the total lipoid-cholesterin concentration of this alcoholic solution is. For diluting, enough of the alcoholic extract is added to normal salt solution sufficient to make the concentration of the lipoids and cholesterin equal to 0.1 mg. per cubic centimeter; five different antigens made in this manner have been remarkably constant in their total lipoid concentration as well as in their anticomplementary and antigenic values.

SURGERY

UNDER THE CHARGE OF

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The Diagnosis of Acquired Diverticulum of the Large Intestine and Sigmoid Diverticulitis.—DE QERVAIN (*Deut. Ztschr. f. Chir.*, 1912, cxxviii, 67) made a study of this subject based upon three cases of sigmoid diverticulitis. In the first, an acute case, the diagnosis was made at operation. In the second, a chronic case, the diagnosis was made before operation. The third case, acute, was seen by an assistant in his absence. When in an old patient acute or chronic disturbances develop in the region of the sigmoid flexure the possibility of diverticulitis should be considered, more particularly when the signs of of acute peritoneal irritation and pain in the left side of the pelvis are present. The diagnosis is made certain with the aid of the rectoscope if one succeeds in passing it high enough. Since the employment of force is forbidden the examination is often unsuccessful. Moreover, peritonitis or a suspicion of abscess will exclude this method of examination. In diverticulitis the *x*-rays can show only the signs of a diverticulitis by the faulty filling of the sigmoid flexure. The proof of the filling of the diverticulum, after partial evacuation of the bismuth injection, is of value in the diagnosis by the *x*-ray. This method of examination of the remains of the bismugh injection permits one to recognize, generally, pathological conditions of the large intestine which can not be recognized either by the administration of the bismuth by mouth nor by the ordinary bismuth injection. The functional *x*-ray examination, that is, the administration of the bismuth by mouth, in diverticulum disease, gives a moderately distinctive picture, only when the feces reach the rectum in a more or less fluid condition. When the feces are firm, the diverticulum does not show clearly, and can give rise to error.

The Influence of the X-rays on the Formation of Callus.—SALVETTI (*Deut. Ztschr. f. Chir.*, 1914, cxxviii, 130) made experimental investigations on rabbits to show the influence of the *x*-rays on bone healing. He concludes that they produce an irritation on broken bone. At first, this interferes with the formation of callus by the production of a large number of cartilage cells and favors their greater persistence. This interferes with the transformation into the osteoblastic tissue, and is a cause of the weakening of its support. The latter effect of

the irritation of the *x*-rays upon the healing of fractures—upon the deposition of lime salts in the bone cells—is not so detrimental. This effect is not, in Salvetti's opinion, dependent upon the other two (the greater production of cartilage cells and their lack of firmness), but is due to special factors brought about by the *x*-ray, which favors the greater accumulation of lime salts. Morpulgo, from his exact and numerous experiments, is positive that the calcifying function of the cartilage cells are in accord with those demonstrated for anabolic and katabolic processes of other substances (fat glycogen). Salvetti believes that if the fracture is exposed to the *x*-rays in the later stages of consolidation, a more effective deposition of lime salts occurs. In this way we can obtain a sure advantage from this property of the *x*-ray, in the healing of fractures, especially in fractures with faulty or delayed consolidation.

Iodin Vaporization in the Treatment of Tuberculous Cystitis.—NORMAND (*Jour. d'Urolog.*, 1914, v, 271) introduces into tuberculous bladders, the vapor of nascent iodine by a special apparatus. It was employed in twenty-four cases and is indicated, particularly, in tuberculous cystitis or tuberculous bladders after removal of a tuberculous kidney. It will give equally encouraging results in cases in which bilateral renal and pulmonary lesions or any other tuberculous focus contra-indicate nephrectomy. It should not be employed in acute attacks of reno-vesical tuberculosis or general tuberculosis, for a time at least. Normand has tried to demonstrate the value of iodin vaporization and to give its exact indications. On the other hand he has tried to overcome the causes of error in the technique of its application and to avoid the painful reactions which constitute the most serious objection raised against the method. It is not claimed to be a panacea against tuberculous cystitis, but he believes it is the most valuable therapeutic agent we have for this affection. If the cures are not more frequent, if he finds it impossible to certify that the cures are permanent, he can, at least, say that there follows a general improvement and relief, and that the method is not accompanied by any danger if it is administered carefully. When one considers the agony which these poor patients experience, whose existence is rendered almost intolerable by the frequent and painful micturition which interrupts sleep and causes a serious drain on the nervous system, the relief afforded by iodine vaporization becomes very important.

Prostatism.—WADE (*Annals of Surgery*, 1914, lix, 321) presents a very valuable study of this subject. He says that three outstanding diseases lead to prostatism: (1) Prostatic hypertrophy or chronic lobular prostatitis; (2) prostatic fibrosis or chronic interstitial prostatitis; (3) prostatic carcinoma. The first is by far the commonest cause (82 per cent. of specimens examined). Chronic lobular prostatitis is a senile hyperplasia, an aberrant overgrowth of tissue, not an independent new growth but liable to develop into the same. Chronic lobular prostatitis usually produces prostatic hypertrophy. It virtually always develops in the middle lobe and is almost uniformly confined to the middle and lateral lobes. The gland, in consequence, undergoes changes that usually permit its easy removal by suprapubic prostatectomy. Chronic

lobular prostatitis may develop in and be confined to the anterior lobe. He observed it in one case. It may cause prostatism without enlargement of the organ, intravesical herniation or complete false capsule formation. In these suprapubic prostatectomy is difficult and dangerous. Its success depends on the presence of advanced hypertrophy due to chronic lobular prostatitis. The recognition of this clinically is frequently very difficult. In the advanced type the urinary tract and general health have usually suffered serious damage from the disease. It is therefore justifiable to delay operation in an early case of chronic lobular prostatitis in order to permit of the gland undergoing those hypertrophic changes that facilitate its easy removal by suprapubic prostatectomy. The mortality attending suprapubic prostatectomy is mainly due to the impaired health of the patient prior to operation. The actual cause of death in such cases is usually a local infection arising out of the wound inflicted. The operation of prostatectomy by blind enucleation is unsuitable in cases of prostatism due to other causes than advanced chronic lobular prostatitis. Perineal prostatectomy is a most suitable operation for such cases. Perineal prostatecomy permits the removal of the disease when its presence is diagnosed in all cases. It is, therefore, at present the operation that offers the best prospect of further advance in the treatment of prostatism. For its successful performance an accurate knowledge of the anatomical structure and relationships of the prostate is necessary as well as an understanding of the pathology of the disease. The suprapubic transvesical route by visual dissection offers the prospect of developing into a method of treating prostatism that may ultimately warrant its adoption in a large number of cases. Chronic interstitial prostatitis is best treated by division and removal of the constriction by the transurethral route. Prostatic carcinoma may be in an early case clinically indistinguishable from hypertrophy due to chronic lobular prostatitis. This fact is therefore a further reason for early operation in all such cases. Prostatic carcinoma when recognized clinically may be successfully treated by excision of the gland in suitable cases.

Operative Intervention in Cystic Disease of the Kidneys.—Mickaniewski (*Jour. d' Urolog.*, 1914, v, 603) says that because cystic degeneration of the kidney is usually bilateral the treatment should be considered as palliative and not curative. It is indicated in intolerable pain, suppuration of the cyst, persistent hematuria, hydronephrosis, displacement of the kidney, and anuria. The function of the supposedly good kidney should be proved to be good by catheterization of the ureters and examination of the urine from each kidney. If the function of one kidney is good, one is justified in doing a nephrectomy. In cases with complications, as suppuration of the cyst, impossibility of fixing a movable kidney, or very abundant and persistent hematuria, no other method of treatment is to be employed. If the kidney supposed to be damaged is considered incapable of performing the whole urinary function, or if the kidneys are simply polycystic, conservative operations are indicated. In case of a suppurating kidney, nephrectomy alone can be employed, but it should be done only if it is absolutely necessary. It should never be done in the presence of anuria. If there is a dis-

placed, large movable kidney, nephropexy should be done and at the same time decapsulation with excision of the cysts. In all other cysts, punctures and incisions of the cysts should be rejected, and the preference given to partial nephrectomy or, better still, decapsulation with excision of all the cysts.

A New Symptom of Fracture of the Patella, with a Contribution to the Treatment.—DREYER (*Zentralbl. f. Chir.*, 1914, xli, 931) calls attention to an interesting observation in a case of fracture of the patella with a considerable separation of the fragments. He applied an extension apparatus with adhesive strips on the Buck principle. The adhesive strips were applied only from the thigh down to the knee, but not over the line of fracture, so that the traction was applied only to the thigh and upper fragment of the patella. He found that with active traction the patient could raise the whole limb, extended at the knee, but this was impossible as soon as the traction was removed. This proved that the lateral expansions of the quadriceps aponeurosis at the knee were not torn, as one would have supposed them to have been torn in an ordinary clinical examination. The fracture was treated conservatively with this traction apparatus in action. After twenty-eight days, with the knee fixed for precaution, the patient could walk about. Eight weeks after admission he could flex the knee to an angle of 40 degrees, could raise the whole limb fully extended at the knee, and could walk up and down steps without support. The Rœntgen ray showed that the separation of 1 cm. at the time of fracture had been reduced to 2 mm., and the clinical examination showed firm bony union. Dreyer believes that with the aid of this symptom (desscribed above) we can diagnose the preservation of the lateral expansions of the quadriceps aponeurosis and thus decide between the cases which must be operated on and those which may be treated conservatively.

The Technique of Gastrectomy.—FINSTERER (*Deutsch. Ztschr. f. Chir.*, 1914, cxxviii, 564) says that in all cases of carcinoma and very small tumors near the pylorus all of the lesser curvature of the stomach to the esophagus should be excised in order to remove the whole lymph-node region of the lesser omentum. The anastomosis between the stomach and duodenum should be made by lateral implantation of the first loop of the jejunum as close as possible to the plica duodeno-jejunalis. By suturing the edges of the opening in the mesocolon to the gastric stump the anastomosis itself is made to sink into the free peritoneal cavity. For the closure of the duodenum it is sufficient to ligate the crushed stump and invert it by a purse-string suture. When the carcinoma encroaches upon the right wall of the esophagus the suture of the latter can be secured by surrounding it, as by a wrist-band, with folds of the fundus of the stomach. Whether a carcinoma is operable or not, it can be decided only by an exploratory laparotomy and a persistent effort at mobilizing the tumor, since the latter can become fixed by old inflammatory adhesions. The enlargement of the regional lymph nodes up to the esophagus does not contra-indicate resection, because the nodes on the one hand are not of necessity carcinomatous and on the other hand by this method can be completely removed.

An exact cleaning out of all the regional lymph nodes is to be done. Resection is justifiable as a palliative operation, since the removal of the foul and bleeding tumor can lead to a more easy and rapid improvement of the patient than can a gastro-enterostomy. It will provide an undisturbed gastro-intestinal function, while in advanced cases the gastro-enterostomy opening will soon be involved in the growth.

Arthritis of the Acromioclavicular Joint as an Important Feature in the Pathology of Obscure Shoulder Injuries.—SIEVERS (*Deutsch. Ztschr. f. Chir.*, 1914, cxxix, 583), in the Trendelenburg Festschrift number, calls attention to the importance of the acromioclavicular joint in the movements of the arm and shoulder. It is frequently affected in obscure shoulder injuries, which are due either to falls on the shoulder or to force transmitted from the elbow or hand. These traumata give rise to degenerative inflammatory affections of this joint, which are demonstrable by the Rœntgen rays in the form of acute or chronic arthritis of this joint. It may be associated with fracture of the acromial end of the clavicle. The condition may exist alone or be combined with other traumatic affections of the shoulder-girdle or shoulder-joint. The diagnosis rests chiefly upon the disturbance of the functions of the joint, especially of its movements. Often there will be symptoms localized to the joint, consisting in demonstrable changes in the joint and subjective disturbances. The Rœntgen rays should be employed in every case and a rœntgenogram of each shoulder should be taken for comparison. The condition causes severe pain and disturbance of movements and long-continued inability to work. The acute form should be treated by rest and novocain injections into and around the joint. The chronic form, in many cases, will resist the usual therapeutic measures. After a sufficiently persistent trial of these, without success, resection of the acromioclavicular joint with implantation of a fatty flap between the ends of the bones will give a satisfactory result. The operation should aim at mobilization and not at ankylosis of the joint.

Original Surgical Uses of the Bone Graft.—ALBEE (*Surg., Gynec., and Obst.*, 1914, xviii, 699) says that his experience as to the trustworthiness of the bone graft, as a surgical agent, when taken with its enveloping membranes (periosteum and endosteum) and contacted with bone, has been borne out by Murphy, McWilliams, and others, who have obtained practically 100 per cent. of successes. In his last 100 cases the successes have been 100 per cent. The endosteum, marrow substance, and periosteum should be included in the graft, as they play a most important role in aiding to establish an early and sufficient blood-supply from the recipient tissues to the cortical part of the graft. The endosteum is also actively osteogenetic as well as the inner layer of the true periosteum. A rapid and complete union between graft and recipient bone should in many cases be enhanced by the interposition of numerous small grafts in which the periosteum may be disregarded because of the easy access of blood-supply to their interior osteoblasts. These coalesce with each other and with the recipient bones and the large graft. The living bone graft has certain

bacteria-resisting properties, as evidenced by two of his animal experimental cases where sepsis occurred and parts of each graft became united to the recipient bones, while the rest of the transplant succumbed to the infection and requestrated. The bone graft apparently acts always as a stimulus to osteogenesis to the bone into which it is ingrafted or contacted. The bone graft when well contacted becomes immediately adherent to the recipient bone by newly formed tissue, which changes to solid bone within four weeks' time. This together with its bacteria-resisting property strongly favors, in Albee's opinion, the substitution when feasible of the bone graft in place of all metal internal splints, especially when it is appreciated that metal has the opposite effect to the graft, in that it inhibits callous formation, produces bone absorption, and favors infection. The dowel, the inlay, and wedge bone graft afford a means of repairing and remodelling the skeleton which the surgeon has not hitherto possessed.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Uterine Carcinoma with Cancerous Ascitic Fluid.—GREEN and KOURAD (*Boston Med. and Surg. Jour.*, 1914, clxx, 352), reports 6 cases of inoperable uterine carcinoma treated by subcutaneous injections of cancerous ascitic fluid. The authors were led to try this method of treatment because of the occasional relief from pain and the temporary retardation of growth that had been observed following similar treatment by Hodenpyl and Risley. An abundance of such fluid was obtained from one of the cases, and with this fluid autogenous inoculations were made in her case and heterogenous in five other patients. The treatment was continued in some instances over a period of four months. The reporting of this series of cases has been delayed for two years, in order to determine as far as possible whether the results obtained were permanent. These cases all showed a slight and irregular elevation of temperature, which, however, bore no apparent relation to the injections of cancerous ascitic fluid, but seemed rather to be due to septic absorption from the ulcerating surface of the cancer. The results obtained correspond with those obtained by Risley at the Massachusetts General Hospital. Three cases gave no apparent reaction; two patients, according to their own statement, were relieved of pain and improved in general physical condition; the third showed an apparent temporary relief of pain, and the tumor sloughed, apparently as a result of the treatment, as evidenced by the passage of necrotic tissue per vagina. Four of the patients died of the disease and apparently without retardation. Two others were discharged and lost to observation. The authors believe that these injections have

a beneficial effect, but whether this effect is due simply to a serum isotonic with the blood and acting as a stimulant or whether the action is specific remains still to be proven. Patients with extensive cancer are usually cachectic and ill-nourished, and therefore it is easy to conceive that the injection of a highly nutritive fluid would have a stimulating effect and aid in improving the general condition and thus probably add to the resistance against the cancer. The authors are of the opinion that the action of such serum is slight, temporary, and shows little or no specificity.

The Influence of Calcium Chloride on Diuresis in Chronic Nephritis. ARNOLDI and BRÜCKNER) *Ztschr. f. klin. Med.*, 1914, lxxix, 300) give their tabulated findings that show that calcium chlorid in small doses is able to cause considerable diuresis in chronic nephritis. This effect was especially observed in cases of nephritis associated with edema and scanty albuminous urine. In order to secure the maximum diuretic action of calcium chloride, they advise that the intake of fluids should be moderate, not over 26 c.c. per kilogram of body weight. The excretion of albumin was not appreciably influenced in 3 cases, in 5 cases the amount of albumin was more or less diminished and in no case was the albumin increased by the treatment.

Artificial Pneumothorax.—SCHAIE (*Jour. Amer. Med. Assoc.*, 1914 lxii, 900) reports 45 cases of pulmonary tuberculosis in which the induction of artificial pneumothorax was attempted for therapeutic purposes. A complete pneumothorax was obtained in 21 cases and a partial penumothorax in 18 cases, while in 6 cases the attempt resulted in failure; 8 cases have given brilliant results. In cases with high fever the results have been most striking. Previously in all these cases there has been persistent fever for periods varying from three to eight months, and the patients had suffered from great loss of weight, chills, and sweats. In all of this group the temperature has remained low or normal since the induction of the pneumothorax, a length of time now varying from six months to one year. In 3 other instances, active and advancing processes have been arrested; 7 cases of hemorrhage were treated, but in one of these cases the attempt to produce a pneumothorax was unsuccessful; 4 patients have had no recurrence of their hemoptysis during periods varying from six months to a year. In one patient the result was partially successful, as the patient has only occasionally spit blood since the operation. Another case has been treated too recently to know what the results will be. It was noted that in 8 cases there was an increase in the signs in the untreated lung; 5 of these had shown a slight tuberculous involvement in the other lung when treatment was begun; the rest apparently developed entirely new processes

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The Technique and Action of Subcutaneous Injection of Neosalvarsan.—WECHSELMANN and EICKE (*Münch. med. Woch.*, 1914, lxi, 535) advise the more frequent use of neosalvarsan by subcutaneous injections. They have given over 7000 such injections without serious accident. They inject from 0.3 to 0.45 gm. neosalvarsan dissolved in 0.5 c.c. of hot 0.7 per cent. salt solution. The most important point

in their technique is to deposit the neosalvarsan solution directly upon the fascia. The details of the technique are given with the precautions necessary to secure this result. When given properly these injections are not painful, and painful infiltrations or abscesses do not result. Toxic symptoms from too rapid absorption of neosalvarsan also do not occur. Wechselmann and Eicke no longer use mercury for the treatment of syphilis, and claim that neosalvarsan is more effectual in controlling the disease.

The Use of Salicylic Enemas in Dysentery.—LUTSCH (*Münch. med. Woch.*, 1914, lxi, 476) has tried Eichhorst's method of treating dysentery by rectal enemas of a 2 per cent. solution of sodium salicylate, with excellent results. He says that pain and tenesmus are both promptly relieved by this method of treatment. The salicylate injections are given at body temperature, and should be retained for half an hour. The dose for an adult is 13 gm. of sodium salicylate in 650 c.c. of water. Lutsch has also used these salicylate injections for the treatment of ordinary diarrheas and catarrhal intestinal conditions, with striking results.

The Danger and the Prevention of Anaphylaxis from Antitoxin.—JOSEPH (*Deutsch. med. Woch.*, 1914, xl, 545) believes that the danger of anaphylaxis in man has been much exaggerated. He does not believe that the phenomenon of anaphylaxis which is observed so frequently in small animals occurs so often in man. The danger of anaphylaxis exists principally in much debilitated children, and when the antitoxin is given intravenously the second time. Joseph thinks that any danger of anaphylaxis could be avoided by using antitoxin obtained from cattle instead of from horses. This could be used for prophylaxis, reserving antitoxin derived from the horse for use in cases of actual diphtheria. Anaphylaxis can also be avoided by inducing anti-anaphylaxis by a preliminary subcutaneous injection of a minimal dose of the antitoxin. This prepares the body in such a way that the injection of a curative dose of antitoxin a few hours later has no power to induce anaphylactic reaction. Friedberger and Mita avoid anaphylaxis by slow intravenous injections of antitoxin, a drop at a time. Joseph claims that any of these methods renders the recipient refractory to any anaphylactic reaction without regard to the method of the administration of the antitoxin.

Salvarsanized Serum in Syphilitic Diseases of the Central Nervous System.—AYER (*Boston Med. and Surg. Jour.*, 1914, clxx, 452) concludes from the use of salvarsanized serum in tabes, paresis, and cerebrospinal syphilis that the method as given by Swift and Ellis is entirely without danger. This method of treatment is effective in many cases where other treatment has failed. It undoubtedly attacks syphilis from the etiological point of view, thus tending to cure the disease as well as relieve the symptoms. The most satisfactory effect of the treatment is seen in the group of cerebrospinal syphilis, in which a complete cure may be obtained in some cases. In tabes arrest of the disease is often possible by this method of treatment, but in general paresis this treatment is least effectual, although in the preparetic

stage encouraging results may be obtained. Ayer is of the opinion that persistent treatment by this method is the most important point in the successful use of salvarsanized serum. Owing to the complicated technique of administration and the necessity to control this treatment by careful examinations of the spinal fluid as to protein content, cell count, Wassermann, etc., Ayer does not expect to see this treatment in general use. He believes it should be employed when other methods of treatment fail in whole or in part, or when haste is required in order to save vital tissue.

Active Immunization against Diphtheria.—SCHREIBER (*Therapie de Gegenwart*, 1914, lv, 97) has applied Behring's method of vaccination against diphtheria to more than 700 school children. No untoward by-effects were noted in any instance, and only occasionally local reactions occurred. Young children and infants gave less local reaction than older children and adults. The intracutaneous method seemed to be the best method of administration. The vaccine is a mixture of toxin and antitoxin, and contains only traces of albumin, so that the danger of anaphylaxis is very slight. Schreiber believes that this method causes a greater production of antibodies than the method of immunization by antitoxin alone. Physicians and nurses frequently exposed to cases of diphtheria gradually become immunized to diphtheria, probably because of repeated mild infections and the consequent increase of antibodies in the blood. The Behring plan of immunization develops a form of active immunity in the same manner.

Salvarsan in Syphilis of the Central Nervous System.—DREYFUS (*Münch. med. Woch.*, 1914, lxi, 525) has used a combination of intravenous injections of salvarsan with mercury and the iodides for the treatment of syphilis of the central nervous system. In some of the cases, details of which are given in the article, very excellent results were obtained. The indications for the treatment are given in detail. Negative findings in the spinal fluid in cerebrospinal syphilis usually indicate that treatment will have no effect. The disease in such cases has become arrested and the symptoms are due to anatomical changes in the cerebrospinal system that cannot be influenced by treatment.

The Mode of Action of Mercury and Salvarsan.—SCHREIBER (*Münch. med. Woch.*, 1914, lxi, 522) is of the opinion that the therapeutic effects of mercury and salvarsan in syphilis can be explained by differing, although complementary, actions upon the virus of syphilis. He bases this belief upon pharmacological and clinical evidence that, according to him, prove that salvarsan kills all the spirochetes it can reach while mercury promotes the immunity reactions. He believes mercury does this by increasing the protective substances in the recipient.

Salvarsan in Syphilis of the Central Nervous System.—IWASCHENZOFF (*Münch. med. Woch.*, 1914, lxi, 530) reports his experiences with the use of salvarsan in 130 cases of various forms of cerebrospinal syphilis. He says that the beneficial effects of salvarsan in such cases is without question. He advises repeated small doses of salvarsan especially

during the early part of the treatment. Initial doses of 0.2 to 0.3 gm. in 100 to 150 c.c. alkaline salt solution were injected intravenously at fourteen-day intervals. In some cases it was possible to increase this dosage, but Iwaschenzoff points out that no definite rules for dosage or contra-indications can be made in the treatment of syphilis of the nervous system. He emphasizes the importance of individualizing the treatment in every case.

The Treatment of Syphilis of the Nervous System by Intrathecal Injections.—CAMPBELL (*British Med. Jour.*, 1914, 2776, 577) says that syphilis is the most common cause of organic disease of the nervous system. When it attacks the central nervous system it gives rise to two sharply differentiated forms of disease, so-called cerebrospinal syphilis and parasyphilis. Campbell prefers to denote these two types of disease as "interstitial" and "parenchymatous" syphilis of the nervous system. Campbell believes that the injection of salvarsanized serum into the spinal canal is the only treatment capable of arresting the pathological process in parenchymatous syphilis. This treatment acts by destroying the spirochetes within the central nervous system and the cerebrospinal fluid. The treatment should be begun as early as possible. Neurons once destroyed are incapable of regeneration. Unfortunately, cases of general paresis and tabes rarely come before us until wide tracts of nervous tissue have been irretrievably damaged. The intrathecal treatment is also indicated in cases of interstitial syphilis, especially of the spinal cord, which do not readily respond to salvarsan, mercury, or iodide of potassium. The latter drug should be given three or four times a day in doses of not less than 60 grains.

Clinical Experiences with Digifolin.—GRABS (*Berlin. klin. Woch.*, 1914, li, 210) has had excellent results with the use of digifolin as a remedy for failure of cardiac compensation. Digifolin may be obtained in tablet or ampoule form, each containing 0.1 gm. of folia digitalis titrate. Digifolin contains the active glucosides of digitalis, but is freed from impurities, especially the safonius and Grabs believes that it is superior to similar preparations derived from digitalis, such as digipuratum and digalen. Grabs found that marked digitalis effect was obtained in cases of mitral cardiac disease, myocardial degeneration and in acute dilatation of the heart. The combination of diuretin and digifolin was very effectual in the more urgent cases with marked dyspnea and edema and in cases complicated with nephritis. Grabs says that no untoward effects follow the administration of digifolin by mouth. After subcutaneous or intramuscular administration, about one-third of the patients complain of slight pain at the site of the injection, but this pain lasts only about an hour. He recommends digifolin because of its stability, the possibility of accurate dosage, its freedom from untoward by-effects and its continued action.

The Palliative Effect of Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis.—VOORSANGER (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1450) reports 14 cases of pulmonary tuberculosis treated by artificial pneumothorax. Voorsanger believes that those cases should be reserved for artificial pneumothorax which do not respond to the

ordinary methods of treatment. Three of this series of cases were in the advanced stages of the disease. They were selected for lung compression to relieve cough, expectoration, and hemoptysis and not with any hope of arresting the disease. Of the remaining 11, 2 patients could not be inflated, 1 on account of adhesions, the other on account of an old pleurisy with effusion. Three of these cases are arrested, 1 patient is rapidly improving and 4 patients are progressing favorably, being inflated at intervals of four weeks. Two patients stopped the treatment of their own volition. All of the cases were, whenever possible, controlled by roentgenograms before operation and before the second inflation. All compressions were made by the Farlanini method with 0.5 per cent. novocain anesthesia. Voorsanger does not agree with those who assert that this operation should only be performed in a hospital or sanatorium. He believes that, whenever possible, it is better to perform the first inflation at a hospital, but that, when a pneumothorax is once established subsequent inflations are simply and quickly performed.

The Indications and Contra-indications for Digitalis Therapy.—Martinet (*Presse Méd.*, 1914, xxii, 301) says, contrary to the general belief that increased arterial tension is a contra-indication to the use of digitalis, that digitalis can be used in many cases to lower blood-pressure. When given for this purpose, the remedy should be given in small doses. A lowering of diastolic pressure is first observed but with continued use, the systolic pressure is often also reduced. Martinet has had very good effects by using digitalis intermittently in small doses in the treatment of angina pectoris. His practise is to give digitalin or digalen for periods of ten days followed by intervals of from ten to twenty days. The administration of digitalis in this way decreased the number and severity of the anginal attacks and invariably lowered the diastolic pressure and often diminished the systolic pressure. Much benefit was also derived in cases of hypertension due to cardiorenal sclerosis, but in this type of disease digitalis was given with shorter periods of intermission. Martinet also found that the administration of small doses of digitalis over long periods of time reduced or caused the entire disappearance of attacks of anginal pain in aortic insufficiency.

Clinical Results with Sennatin.—Lindborn (*Münch. med. Woch.*, 1914, lxi, 872) writes concerning sennatin which was introduced by Credé as a cathartic suitable for subcutaneous or intramuscular use. The average dose is 3 c.c. and no untoward effects have been observed from its subcutaneous or intramuscular use except, in some instances, a transient rise of temperature. Lindborn tried this remedy in 46 patients. He found that it had a distinct effect in increasing peristalsis in 80 per cent. of this series. In 62 per cent. the increased peristalsis was sufficient to produce a movement of the bowels. In 14 of the 46 patients, a single injection of the remedy had a continued action; the patients who formerly never had a movement of the bowels without an enema had spontaneous daily evacuations for periods as long as a week.

OBSTETRICS

UNDER THE CHARGE OF

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Repeated Tubal Gestation with Blood Cyst of the Ovary; Operation; Recovery.—BUTLER-SMYTHE (*Jour. Obs. and Gyn. British Empire*, February, 1914) reports the case of a patient taken with typical signs of ectopic gestation, and operated upon. On opening the abdomen the left tube was much enlarged and the left ovary large and cystic. The patient recovered from the operation, and the specimen consisted of left tubal gestation and a blood cyst of the left ovary. Two years after the patient was taken suddenly ill with symptoms of ectopic gestation with internal hemorrhage. As this had evidently ceased there was delay of twenty-four hours to prepare for operation. When the abdomen was opened a large quantity of dark fluid blood was found and ectopic gestation in the right tube. On examining the specimen the tube showed chorionic villi, the right ovary was a cyst containing dark fluid blood. The patient ultimately made a complete recovery.

Three Atypical Cases of Postpartum Pyelitis.—MURRAY (*Jour. Obs. and Gyn. British Empire*, February, 1914) has treated 8 cases of severe pyelitis commencing after labor. In 5 the diagnosis was easy, with changes in temperature, pus in the urine, and kidney tenderness in 4. In 3 cases there was total absence of local signs and symptoms, temperature remittent rather than intermittent, absence of chills, smaller amount of pus in the urine, although the patients were seriously ill, and the disease beginning on the day following labor. The first case was a primipara with delivery in breech presentation, followed by fever. The urine contained pus and coliform bacteria. The patient gradually recovered. A second case, a primipara, had forceps delivery followed by fever, without signs of uterine infection. The patient had acid urine, 4.5 per cent. of glucose, pus, and coliform bacteria. She died of coma a few days after delivery, and diabetes was thought to complicate the infection by the colon bacillus. The third case, a multipara, gave natural birth to a premature stillborn child. Her symptoms resembled enteric fever with absence of symptoms of streptococcus uterine infection. The blood was negative to the Widal test and culture test for bacillus typhosus. The urine showed the usual signs of colon bacillus infection. A vaccine was prepared from the coliform organism, obtained from the urine, and this produced very steady improvement. In using the vaccine, Murray has found by observation that each patient must be treated individually, and that the dose must be varied in accordance with the nature of the case. In acute pyelitis, a first dose may vary between 3,000,000 and 30,000,000 of autogenous coliform organisms. If no improvement follows such

dose must be rapidly increased at intervals of a day or two until the improvement occurs. The greater the intermissions of temperature, the smaller must be the dose. Where fever was high and continued, 30,000,000 was given as a first dose, increased within two weeks to 250,000,000. Where alkalies or urotropin are used, tests should be made to ascertain whether formalin is really produced. Acid sodium phosphate in half dram doses, three times daily should be given. Urotropin should be given in tablet or powder alone. After a preliminary small dose as a test this drug should be pushed to 20 or 25 grains, three times daily.

The Treatment of Eclampsia by Euphyllin.—LICHTENSTEIN (*Zentralbl. f. Gyn.*, No. 23, 1914) states that he has obtained good results by the employment of euphyllin. This substance is a combination of theophyllin and ethylendiamin. It is 40 per cent. soluble in water and contains 78 per cent. theophyllin. Its solubility makes it very adaptable for injection and it works promptly and efficiently. In 5 cases of eclampsia where the secretion of urine was almost suspended, this substance injected into the muscles in doses of 2 c.c. produced great increase in the diuresis.

Uncontrollable Uterine Hemorrhage.—In the *Jour. Obs. and Gyn. British Empire*, March, 1914, BRIGGS AND HENDRY contribute an interesting paper, giving the results in the examination of 104 uteri removed by hysterectomy for uncontrollable bleeding. The writers conclude that uncontrollable uterine hemorrhage is a functional disturbance; the disturbers local and general, numerous and varied. Among them, arteriosclerosis, fibrosis uteri, chronic metritis, and chronic infective endometritis have been rated too highly and considered too important in pathological treatment. For two or three weeks after an early abortion, curettage may remove successfully the friable relics of conception, but in other cases the use of the curette fails, and many erroneous diagnoses of endometritis result. In both treatment and exploration curettage is uncertain in success and failure. Chronic appendicitis with growths in the uterus, and retention of growths of conception may cause uncontrollable bleeding, when the uterus itself is not at fault. The real pathology of cases is often obscure, as a case where hemorrhage at menstruation has been increasingly great, after a brief period of amenorrhea, followed by an unrecognized case of early abortion, is diagnosticated as a case of metrorrhagia. Examination may show a small placental polyp is present. The case becomes clearer if one remembers that in this particular instance the average abortion rate, 15 to 17 per cent., had not been exceeded, and that sterility occurring usually in 5 of 95 married women, was below the average rate. The paper is accompanied by illustrations.

Chorio-epithelioma with Difficulty of Diagnosis.—WILLIAMSON and NOON (*Jour. Obs. and Gyn. British Empire*, March, 1914) report the case of a multipara who expelled a vesicular mole after three months of amenorrhea. A month after she had fever and abdominal pain, and six weeks after the expulsion of the mole an abscess was opened and drained through the vagina. Four months later she was well.

About a year after, menstruation ceased and she was taken with sudden abdominal pain, loss of appetite, vomiting, constipation, and loss of weight. After some weeks she coughed up frothy, blood-stained mucus. On admission to hospital the patient was jaundiced, the tongue furred and dry, temperature 99° F., pulse 108, respirations 40. The breathing was shallow, the left side of the chest moved imperfectly, percussion was dull, and breath sounds weak over the left lung. The lower abdomen was distended. A tumor extended out of the pelvis seven inches above the pubes, and very clear souffle could be heard over its right upper border. The tumor was elastic, slightly tender, and not fixed. Liver dulness seemed normal. On vaginal examination there was a round, tender, elastic mass in the pelvis, from which the uterus could not be separated. The cervix was high up behind the symphysis, the tumor encroached upon the bowel, the urine contained bile, and the blood examination showed 3,500,000 red and 10,000 white cells. *x*-ray examination showed dark areas indicating deposits in both lungs. Abderhalden test was then applied for both pregnancy and carcinoma, with placental tissue. The result was strongly positive by the ninhydrin test and the optical method. With carcinoma tissue the result was negative, and diagnosis of chorio-epithelioma was made. Twenty days after admission the patient died with failure of respiration. Autopsy confirmed the diagnosis.

The Practical Relation between Maternal and Fetal Blood.—VOLLHARDY (*Zentralbl. f. Gyn.*, 1914, No. 20) has studied the blood from the mother and from the umbilical cord to ascertain the difference between them, and what test gives a practical result. He finds that the test with acids or platinum chloride shows a marked difference between these two substances and that this can be applied to the dry blood. Fetal blood may be recognized as giving a negative reaction to the test even when an alcoholic extract of the blood has been made. The Abderhalden method was tried and was found unreliable.

The Final Results of Ectopic Pregnancy.—SMITH (*Surg., Gyn., and Obst.*, June, 1914) has studied the results obtained in 192 cases operated upon for ectopic pregnancy, and their condition five years after operation. He finds that in 145 cases the general health is described as good. The final result then, so far as the general condition of the patient is concerned, was very satisfactory. In 144 cases in whom pregnancy might have occurred after the operation, 97 remained sterile. As regards the recurrence of ectopic pregnancy, of the 192, 48 had abortions or were in such condition that recurrent ectopic pregnancy could not take place. Of the 144 in whom pregnancy could happen, 47 had uterine pregnancies, 42 with living children, 64 children in all; 1 stillbirth, 5 aborting without children, 5 abortions and children. Among these there were 21 cases of repeated ectopic pregnancy, half as many as had living children; 2 of these patients had subsequent children and also ectopic pregnancy. Of the 67 women aged under thirty years, 27 had subsequent uterine pregnancies, of whom 10 had repeated ectopic pregnancy. Of the 74 women aged above 30 years 19 had subsequent uterine pregnancy and 11 had repeated ectopic pregnancy.

Essen-Möller finds 46 per cent. of patients operated upon for ectopic

pregnancy, have children subsequently. Prochownik 43.8 per cent., Smith 32.6 per cent., and of these in Smith's series 14.6 per cent. had repeated ectopic pregnancy. Under these circumstances, when operating upon a case of ectopic pregnancy of tubal origin, should the opposite tube be left? To do this certainly exposes the patient to the possible risk of repeated ectopic pregnancy, and yet to remove both tubes destroys the possibility of pregnancy. Smith believes that the age and general strength of the patient, her circumstances and her own convictions in the matter must be carefully considered. In some cases it is far wiser to remove both tubes, in others this should not be done.

The Abderhalden Test for Pregnancy.—WALLIS (*Jour. Obs. and Gyn. British Empire*, February, 1914) reviews extensively the literature upon this subject. He adds his own experience in testing the sera of 50 women known to be pregnant. Of these, 20 were in the last three months, or had recently been delivered. In each case the optical test and the test by dialysis were positive. The remaining 30 were in the earlier months of pregnancy, from the eighth week to the fourth month, and gave a positive reaction. In 30 non-pregnant women the reaction was negative to both tests; 8 of these patients had cancer and 14 syphilis. The sera of 30 males were tested by both methods, with negative results. A large number of these men had syphilis. In 110 cases the test was correct. In 8 cases the sera of patients with cancer digested cancer tissue, but did not digest placental tissue. The sera of 5 cases with tuberculosis were tested with emulsion of human tubercle bacilli with positive results. One case of tuberculous salpingitis gave a positive reaction with the emulsion, a negative with placental tissue. The controlled sera in 10 cases gave negative results to tubercle, including one case of hydrosalpinx, found at operation not tubercular. Repeated attempts to use the test in the diagnosis of syphilis have failed. In 18 cases with various complications the test was made and the optical method was correct in each; 3 had suspected ectopic gestation; 6 had tumors where pregnancy in addition was suspected; 3 had chorio-epithelioma, 1 cholera, 1 heart disease with amenorrhea, 2 nephritis, 2 puerperal sepsis. In 2 cases of inflammation of the tubes the test by dialysis failed; no optical test was made. The test is essentially for the presence of chorionic villi, and will be positive so long as these remain in the body of the patient in contact with her blood. There will probably be valuable aid given by this test in studying the toxemias of pregnancy and the ferments formed by the liver and kidneys. At present Wallis believes that it has been fairly established that the serum of pregnant women contains a specific ferment capable of digesting placental tissue, and this ferment can be detected from the eighth week of pregnancy until ten days after delivery by the optical and dialysis methods. Both tests should be used in the case and the accuracy of the results obtained by the most scrupulous care in details of the method. These tests are of value in diagnosis in the early diagnosis of pregnancy; the differential diagnosis between fibromyomas and pregnancy, the diagnosis of ectopic gestation, of chorio-epithelioma, and retained placenta. At present there is no reason for believing that the serum of pregnant women will digest other than placental tissue.

GYNECOLOGY

UNDER THE CHARGE OF

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PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Pathology and Treatment of Chronic Leucorrhea.—In a continuation of the work reviewed in this department a few months ago, CURTIS (*Surg., Gyn., and Obst.*, 1914, xix, 25) gives some of his deductions as to the etiology and best methods of treatment of leucorrheal discharges. He believes that in the vast majority of cases, vaginal discharge in a non-parous woman is of gonorrheal origin, even if the gonococcus be no longer demonstrable by any known method; in women who have borne children, however, other factors come into play, such as altered anatomical relations, loss in elasticity of the tissues, etc., so that the gonococcus cannot always be held responsible. As was stated in the previous paper, the author firmly believes that the usual seat for the formation of purulent discharges is the lower genital tract (lower cervix, vagina, vulva), the endometrium remaining uninvolved. The indications for treatment he resolves into the following categories: (1) Improvement of the lowered resistance of the genitalia, which often exists, by improving the general health of the patient, proper attention to the bowels, repair of any lacerations present, correction of displacements, etc. (2) Avoidance of measures which are not only useless but often harmful; among these Curtis classing curettement, douches, and tampons. (3) Reduction of the mucous discharge from the cervix, since this forms an excellent culture medium for any bacteria present, and thereby plays an important role in the production of leucorrhea. While theoretically operation, with actual excision of all glandular tissue, might be advisable, scarification, or the repeated application of strong silver nitrate (20 per cent. solution) to the cervical canal, have proved satisfactory measures in most cases. (4) Application of the same solution to urethral granulations, Skene's and Bartholin's glands, or the excision of the latter, to remove thoroughly all residual gonococci. (5) Vaccine and powder treatment; vaccine therapy was given a thorough trial, autogenous vaccines, made from what appeared in each individual case to be the predominating organism or organisms, being used; in many instances these were of the anaërobic group. Injection was started with low doses—10,000,000 to 20,000,000—and rapidly increased to from 150,000,000 to 300,000,000 at a time. While the results in a number of patients appeared favorable at first, as a rule the symptoms subsequently recurred and were then apparently uninfluenced by treatment. A thorough trial was also made of a large number of the various drying powders and yeast preparations, so strongly advocated by the Germans, with again irregular, and on the whole, disappointing results. Temporary improvement was the rule, irritation and discharge lessening during treatment, but only to recur in many instances upon its cessation.

Massage Treatment of Pelvic Inflammations.—In an article entitled "Twenty Years of Gynecologal Massage," DELASSUS (*La Gynecologie*, 1914, xviii, 81) makes a strong plea for a more careful consideration on the part of the profession of this form of physiotherapy, which he says he is convinced, after many years' experience with it, often is able to replace operation, and to restore more or less invalid women to a condition of functional health. He claims no particular originality for what he has to say, but merely wishes to point out some of the essential details, the ignorance or non-observance of which has often led to disappointing results, and therefore to disgust with the entire method. The only apparatus required for the proper application of gynecological massage is a fairly firm table or couch, of sufficient height to permit the operator to reach the patient without discomfort. Upon this the patient lies in the dorsal position, with the knees drawn up, and the clothing sufficiently loosened about the body to permit of free access to the abdominal wall; it is well to place a small pillow under her head and another under the lower part of the spine. Standing at the left side of the patient the physician gently introduces the index finger of his left hand into the vagina; this serves merely for support and counter-pressure in the subsequent manipulations, which are in most cases carried out entirely by the right hand placed upon the abdomen. At first only very gentle manipulations—pressure along the muscles, superficial strokings, tappings, rubbing, etc.—should be made, at a distance from the site of the chief lesion, just as one would massage at first gently around an inflamed joint or a fracture. Later, deeper pressure may be made, but throughout all semblance of violence is to be rigorously avoided. If much pain is caused it indicates either that the lesion is still too acute and the treatment should be postponed, or if the lesion is chronic that this form of therapy is contra-indicated. The author emphasizes the fact that patience is the key-note in the successful application of this treatment, and is required of both doctor and patient. The chief difficulty met with at first is usually the resistance of the abdominal muscles; even with the best of will, the patient is often unable to overcome this. No attempt should be made to conquer by force, but rather by gradually distracting the patient's attention and winning her confidence. Each seance should last at first about five to six minutes, gradually increasing up to a quarter of an hour. The best results are obtained if treatments are given daily, though often this is impossible; they should under no circumstances be farther apart than three times a week, however. *Indications:* The author is distinctly conservative in this respect, and does not attempt to draw all forms of gynecological disease into the realm of massage therapy. He gives the following as the type of case *par excellence* in which it is indicated: A young woman (twenty to thirty-five years) who has had two or three children, or several miscarriages, who now complains of irregular and painful menstruation, moderate leucorrhea, indefinite pains in the groins and lower abdomen, and a feeling of heaviness and general malaise; is nervous, irritable, upset at the least little domestic worry, and generally below par. Such patients, upon examination, are usually found to be exceedingly tender to vaginal pressure, even before the adnexa are reached; the latter are slightly enlarged and very tender to bimanual palpation. The condition,

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an exceedingly common one, is a chronic salpingo-oöphoritis with pelvic cellulitis. The first effect generally noted from massage treatment in such a patient is a relief of the heavy feeling in the abdomen, then gradual disappearance of the pains and tenderness, reëstablishment of regular and painless menstruation, often relief of dyspareunia, etc. In starting a course of treatment, however, no definite promises should be made, and unless distinct pain is caused, or the patient is getting worse, it should be tried for at least two weeks before forming any judgment as to its efficacy; if improvement is noted it should then be continued until a definite cure is attained or a status quo is reached, beyond which no further progress is made. Delassus believes that in most instances the cure is symptomatic, rather than a true return of the diseased organs to a normal anatomical condition, but he reports one case of a woman who was sterile for thirteen years after the birth of her first child, but who became normally pregnant some months after undergoing massage treatment, and another instance in which a woman who had had five successive miscarriages at about the second month was enabled to go to full term, indicating at least that a functional *restitutio ad integrum* may occur. In some instances the symptomatic cure is apparently permanent; in others recurrence takes place, and further series of treatments become necessary or operation may be indicated. The author admits that he cannot give a scientific explanation for the results obtained, but suggests that they may be due to an emptying of congested bloodvessels, excitation of vasomotor centres, and consequent relief of edema and congestion.

Conservative Surgery of Benign Ovarian Tumors.—FREUND (*Zentralbl. f. Gyn.*, 1914, xxxviii, 985) has devised a method for the preservation of some functionating tissue in operating for even quite large tumors or cysts of the ovaries in cases where this seems especially desirable. Although many operators have practised to a greater or less extent partial resection of the ovaries under certain circumstances, they have for the most part limited the application of this process to small growths or inflammatory conditions, and have generally been content with preserving a portion of the hilus, believing that any functionating ovarian tissue left is most apt to be situated in this region. Freund has found, however, that while this generally holds true it by no means always does so, some cysts, for instance, developing in the hilus, and pushing the only bit of undestroyed ovarian tissue to the farthest pole, or some other portion of the surface of the tumor. In such cases, therefore, as appear suitable for conservative surgery, Freund proceeds as follows: After opening the abdomen the entire or partially evacuated tumor (cyst) is delivered through the incision and completely packed off from the abdominal cavity. The tumor is then bisected throughout its extent, the pedicle being grasped in the left hand. After the contents are thus evacuated every point of the wall can be quickly examined by the eye and finger, and any remaining area of normal ovarian tissue quickly localized. If this is found near the pedicle the tumor is simply cut away in such a manner that the tissue to be preserved is left in contact with the pedicle, which is then sewed over with a fine suture. If the ovarian tissue is on the periphery of the tumor, however, a thin strip of tumor capsule is left between the pedicle and the ovarian remnant;

thus the latter is maintained, while the growth is completely removed. It is, of course, important that the ovarian artery shall not be tied, but this is not necessary, as the hemorrhage is generally very slight. The chief indications for this operation are found in cases of bilateral benign growths, such as pseudomucinous cystomas, follicular and corpus luteum cysts, and dermoids occurring in young women. The author reports that in all cases upon which he has performed it (running back over three and one-half years) menstruation was preserved and no signs of the artificial menopause occurred. As yet he is unable to report the subsequent occurrence of pregnancy, but hopes to ge able to do so in the future.

OPHTHALMOLOGY

UNDER THE CHARGE OF

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Paralyses of the Motor Oculi in Otitis and Sinusitis.—BERARD, SARGNON AND BESSIERE (*La Clin. Ophtal.*, December 10, 1913, p. 698) find that isolated complete paralysis of the third nerve in chronic otitis is extremely rare compared with the much greater frequency of isolated paralysis of the external rectus described by Gradenigo. Besides a lesion of compression in cerebral abscess, isolated and complete paralysis of the motor oculi may be due to a lesion of the anterior part of the petrous, and especially of the external wall of the cavernous sinus. Intervention may be attempted, but the prognosis is very grave. In the course of frontal, ethmoidal, sphenoidal, and even maxillary sinusitis, isolated partial or total paralysis of the third nerve may occur; the partial variety is of favorable prognosis, but the total form is much graver; the latter may, however, recover, sometimes even spontaneously.

Treatment of Squint.—V. GROSZ, in an address before the Belgian Society of Ophthalmology (*Klin. Monatsbl. f. Augenhk.*, September, 1913, p. 424), advocates commencing treatment at the earliest age by the continued instillation for several months, in both eyes alternately, under constant medical control of a 1 per cent. solution of atropin. With intelligent children stereoscopic exercises should be begun early. The wearing of properly correcting glasses is of importance. As regards operation, there is no need for haste, unless for special reasons it may be delayed until the eighth or tenth year. In many cases of convergent strabismus, particularly the alternating form, simple tenotomy will be sufficient. The author does not agree with the view that this operation may be dispensed with or that it is injurious. In divergent stra-

bismus, where the deviating eye is, as a rule, amblyopic, tenotomy is of little service and advancement is to be preferred. In the discussion, de Lapersonne (Paris) shared the view that operation should not be performed in convergent strabismus before the tenth year. He likewise has not abandoned tenotomy, although he regards advancement as holding the first place. Following operation binocular vision is frequently remarkably improved and can be further developed with the diploscope. Jessop (London) likewise does not operate before the tenth year and performs advancements only and highly values alternate atropinization in young squinters.

Hypophysis Tumors.—Fleischer (*Klin. Monatsbl. f. Augenhk.*, vol. lii, p. 625), from an analysis of fifteen cases, finds that visual disturbance when once begun almost invariably led to blindness in the course of a few years. Hemianopic temporal defects were present in every instance. Two cases operated by Schlöffer's method and one by von Hirsch's ran an extremely favorable course. In one case there were no further morbid phenomena, and the patient was able to return to work, as was also the fact in a second case. In a third the nasal half of the field was recovered. Operation is accordingly to be insisted upon, especially if there is provisional loss of visual acuity.

Treatment of Luxations of the Crystalline Lens.—Ask (*Klin. Monatsblatt. f. Augenhk.*, September, 1913, p. 331), based upon pathological, anatomical, and clinical experience, argues that the intrabulbar luxated lens constitutes a permanent threatening danger for the eye and should accordingly be removed whenever possible. He especially insists that his own pathologico-anatomical findings in subconjunctival luxations urgently bespeak early operation (enucleation if necessary,' and this with regard to the danger of sympathetic opthhalmia; otherwise, as a rule, early removal of the subconjunctivally luxated lens) and against the views of Stellwag, Manz, and Mackenzie, which are still prevalent today, that to favor consolidation of the scleral cicatrix extraction of the subconjunctivally luxated lens should be postponed for a considerable period.

Fibrolysin in Stricture of the Lacrymal Canal.—Wolffberg (*Woch. f. Therap. u. Hyg.*, 1913, No. 44, p. 398) confirms the statement of P. Cohn regarding the beneficial action of injections of fibrolysin. He has treated satisfactorily ten cases of blennorrhea of the lacrymal sac with strictures impervious to the smallest probes. After thorough cleansing with hydrogen peroxide he injects with the Anel syringe a little suprarenal-cocaine solution, following which a few drops of fibrolysin are deposited in the same manner upon the strictured point. In a quarter of an hour in one case reported a probe could be introduced and passed smoothly the following day. Fourteen days' treatment resulted in cure. The writer particularly emphasizes the rapidity of action of this medicament.

The Eye-ground in Psychoses.—Benedict (*Annals of Ophthol.*, April, 1914, p. 233), from a study of the fundi of psychopathic subjects, concludes (1) that well-defined disorders from extensive morbid con-

ditions may exist for sometime without change in the ophthalmoscopic appearances of the eye-grounds; (2) cases of dementia precox, either slowly developing or rapidly deteriorating, present no associated disk changes peculiar to this condition, but rather a higher percentage of normal fundi than either the organic or functional group of psychoses; (3) in functional psychoses there is no definite association between the mental disorder and the ophthalmoscopic appearance of the fundus.

The Scientific Basis of Potassium Iodide in Arteriosclerosis.—FLURY (*Archiv. of Ophthal.*, July, 1914, p. 405) summarizes the results of experimental investigation as follows: The drug has a pronounced salt action, whereby it modifies osmotic processes and increases cellular activity. In addition the specific effect of the ions must be regarded. The potassium by its action on the central nervous system and muscles facilitates the transport of the salt in the tissues and the exchange of ions, and also causes special changes in the mineral metabolism. The peculiar distribution of iodine in the body shows that it has a distinct affinity for certain tissues. As regards arteriosclerosis, the arterial vessels as well as the glandular cells and many diseased tissues are able to collect iodine. The therapeutic use of iodide of potash may not only influence metabolism, but directly affect the vascular elements in arteriosclerosis. The reduction of the friction of the blood which potassium iodide causes may result in an improvement in the circulation and increased diapedesis. It may also be assumed, from the known effects of poisoning with iodine in man, that the reduction of blood-pressure plays a role in the action of the remedy. Iodide of potash cannot be replaced by any other salt or any of the numerous modern substitutes, inasmuch as its therapeutic effect depends upon the salt, the potassium and the iodine, of which the latter is probably the most important.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

How Salivary Secretion is Influenced.—WERTHEIMER and BATTEZ (*Jour. de Physiol. et de Path. Gén.*, November 15, 1913, vol. XV, No. 6) have undertaken experiments to decide the question of how the salivary glands are stimulated to secretion. It will be remembered that Cohnheim and Lichtheim found that salivary secretion increased if saline solution was introduced into the circulation. They considered that salivary secretion was one means by which the body cleared itself of the excess of fluid. Later Cohnheim found that even

without the assistance of the secretory nerves a hydremic condition led to an increase of the secretion, and sometimes to a distention and edema of the glands, and thought that these manifestations were entirely separate from the nervous system; he went further, and having paralyzed the chorda tympani by atropin, he still found that injection of saline was efficient in producing edema of the gland. Hamburger considered that there could be no salivary secretion without nervous excitation, and thought that the reason why solutions of certain salts caused salivation was by the eliminated salts impresssing the gustatory nerves. The authors think that gustatory excitation plays no part in the provocation of salivary secretion by the injection of salts, for after section or paralysis of the gustatory nerves, as well as after the injection of pure and distilled water, the salivation was obtained. They consider that the reactions of the submaxillary gland, either intact or deprived of its nerves, show that the secretion following transfusion of liquids into the blood is almost entirely under control of the central nervous system excited directly by the heightened blood-pressure. Such excitation they consider is transmitted by the chorda tympani. Compression of the abdominal aorta, which increases the pressure in the subdiaphragmatic region, has the same result, although less marked, as follows the injection of saline, especially in animals whose blood is already in a hydramic state.

Carrot-juice Agar as a Medium.—Rochaix (*Jour. de Physiol. et de Path. Gén.*, November 15, 1913, vol. xv. No. 6) finds that carrot-juice agar is an extremely useful medium for the growth of colon, typhoid, and paratyphoid of many sorts, of which it gives abundant cultures in twenty-four hours at 37°. It is equally applicable to Bacillus pyocyaneus, anthrax, Streptococcus pyogenes, and the encapsulated group, while, on the contrary, it is unfavorable to the development of staphylococcus, diphtheria, and pneumococcus. It is made as follows: carrots well washed are cut up and the juice expressed; 200 c.c. water is added to 800 c.c. of carrot juice, and agar is added, as in the preparation of ordinary peptone jelly, in the proportion of about 30 to 35 grams per 1000 c.c. The mixture is kept at 115° for twenty-five minutes in the autoclave; clarified with white of egg; alkalinized, and filtered. After being tubed it is sterilized again at 108° to 110°, after which the medium is more clear and transparent than the ordinary peptone jelly. The author has used also carrot juice, agar glycerinated, artichoke agar, potato agar, and beet-root agar, but finds that, everything considered, the first named is the best, for the reason that with simple economical preparation and absence of peptone it is yet possible to obtain luxuriant growths of the bacilli indicated, and very rapid growths of molds; while the production or absence of gas in the agar cultures is another differential characteristic which can be added to those already known as separating the colon-typhoid group from the encapsulated forms.

The Frequency of Tuberculosis.—Lubarsch (*Virch. Arch.*, 213, 417) publishes autopsy figures which are authoritative from Posen, Zurckau, and Düsseldorf, showing that tuberculosis was present in 57.4 per cent. of 7371 cases, whereas it was found in 69.2 per cent. of 5800 adolescents.

Orth adds as a footnote that 51.4 per cent. was the figure for his own institute (1000 autopsies in Montreal gave a total tuberculosis figure of 43.7 per cent.). Since the figures for latent and healed tuberculosis were higher in adolescents than in all cases, the conclusion appears to be justified that the tendency to healing and to a harmless course is greater in the former. Further, in 1114 cases Lubarsch was able to determine a hematogenous source for 29 per cent.

Plasma Cells in the Kidney.—CEELEN (*Virch. Arch.*, 211, S. 276, 1913) has examined a series of 60 kidneys, mostly from the young, some from the newborn. His contention is that plasma cells are never found in the normal kidneys, and nearly always in the damaged organ, save perhaps in cases of simple hyperemia; in pyelonephritis they are likely to be especially prominent, and they may be so numerous in interstitial nephritis as to merit the statement that in primary interstitial nephritis (if one allow the term) there is a plasma-cell stage. The cells are found in the periphery of the veins and arteries and above the Malpighian bodies. They vary greatly in size and may be multinucleate. They are histiogenous, originating from the capillary endothelium, from adventitions cells, but probably not from hematogenous lymphocytes. They may give origin to smaller round, plasma daughter-cells. They may be found in the blood; they give us specific indication of disease, save that in the newborn they are characteristic of syphilis.

An Unusual Form of Meningeal Tuberculosis.—VON CZIRER (*Centralbl. f. allg. Path. u. path. Anat.*, Bd. xxv, No. 4, 28, February, 1914) describes a very unusual form of meningeal tuberculosis which occurred in a man aged twenty-five years; a flattened, outspread mass of pale reddish-gray color and 0.5 cm. thick lay over the convexity of the left hemisphere. It measured 8.5 by 5.7 cm., and broadened out over the posterior part of the frontal lobe and the front part of the parietal. Macroscopically it was judged to be a sarcoma, but its microscopic examination determined a tuberculous character, and the specific bacilli were found in the sections. It is very unusual to find a departure from the usual basal inflammation, and Czirer has found only two or three cases reported.

Market Butter.—In a study of the market butter of Boston by ROSENAU, FROST, and BRYANT (*Jour. Med. Res.*, March, 1914) there are one or two points of interest to the casual reader. All the specimens tested would be classed as good butter, and, it may be remarked in passing, passed the necessary standards. Twenty-five samples averaged five and a half million bacteria per gram, and the authors state that the bacteria diminish markedly with age of the butter in which they are contained. One sample diminished 85 per cent. in two weeks, two others over 90 per cent. in four and six weeks. Bacillus coli appeared occasionally, streptococci frequently, and B. welchii not at all, although this last is frequent in milk. Tubercle bacilli were found in two of twenty-one samples, which gives a figure corresponding closely to the number of milk samples similarly inspected. The authors consider that the cream used for butter should be pasteurized, the

more so as general high quality of butter is no guaranty of safety in this regard; the samples which contained tubercle bacilli were, in fact, the most high-priced and generally excellent samples in other regards.

The Eosinophilic Granules.—Miller (*Centralbl. f. allg. Path. u. path. Anat.*, Bd. 25, No. 6, March 31, 1914) takes up the ill-understood subject of the natures of the eosinophilic granules. He is strongly opposed to the idea that these originate from hemoglobin or are of hemoglobin nature; they are to be found in low forms of life which possess no red corpuscles, they contain no hematin group; a change of fragments of erythrocytes into these granules has never been observed, and eosinophiles do not give origin to pigment cells; even staining differences are to be observed between these and hemoglobin particles. The granules, moreover, are in direct connection with the stroma of the cells. Nor, thinks the author, are these granules of the nature of the bodies known as Russell's fuchsin bodies, which are found very exceptionally in plasma cells. Miller considers that the presence of eosinophiles has no diagnostic value in the differential diagnosis of gonorrheal disease of the adnexa.

Salvarsan and Other Therapeutic Agents as Antiseptics.—Schiemann and Ishiwara (*Zeits. f. Hyg. u. Infektionskr.*, Bd. 77, Hft. 1, 1914) have conducted painstaking labor upon the antiseptic qualities of salvarsan and ethylhydrocuprein, and they find that *in vitro* these agents prevent growth in dilutions of one in a million. The actual killing power of salvarsan exists in such dilution, but is excited slowly so that at the end of twenty-four hours the height of the action may not be reacted. The drugs are selective, also, salvarsan being effective on the authrax, glanders, and erysipelas organism, cuprein on pneumococcus, the effect on various other bacteria being lessened a hundred and even a thousand fold. In serum, the effects are not greatly different from those observed in bouillon, activated serum permitting a greater effect than inactivated, which is the opposite result to that found in the case of sublimate. Phenol is weakened by serum to a less degree than is sublimate. The effect of salvarsan differs according to the kind of serum, cattle serum giving a less potent result than rabbit serum. The authors explain the differences seen in salvarsan and cuprein on the one hand, and sublimate on the other, as the result of the lipoids in the serum. Lecithin and cholesterin added in a strength of 1 in 100 caused a very marked weakening of the ability to prevent growth of bacteria.

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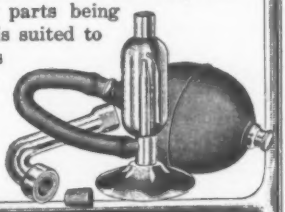

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